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PENICILLIN THERAPY IN OPHTHALMOLOGY

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Reports on the use of penicillin appear in increasing numbers in almost all fields of medicine. Certain properties of the substance explain the hope for its therapeutic effectiveness which is shared by all members of the medical profession: first, its bacteriostatic action in high dilutions against many species of organisms, especially pyogenic cocci, gonococci and clostridiums; then, its low tissue toxicity, and, last, the great solubility and diffusibility of the salts of the compound.

Because of these qualities it is not surprising that the first paper published by Florey and his co-workers [1] on the practical use of penicillin in general included 4 cases of ophthalmic disease. In a second publication, Florey and Florey [2] reported satisfactory results from treatment with penicillin of a series of infections of the lid border, the conjunctiva, the cornea and the tear sac. In a number of these cases, which were selected by Ida Mann, treatment had been carried out unsuccessfully for a long time with other drugs. By applying a cream containing 100 units (Oxford) per gram to burns of the eyelids and conjunctiva, Bodenham [3] eliminated pyogenic cocci from the granulating wounds. Sorsby [4] studied the effect of penicillin in a few cases of ophthalmia neonatorum. When the infecting organism was the gonococcus, results were more dramatic than those obtained with sulfanilamide. Lyons [5] and Berens [6] found that cases of nonspecific iridocyclitis and chorioretinitis were not significantly influenced by systemic penicillin therapy. Cashell [7] collected a series of penicillin-treated eyes and confirmed Florey's favorable results in treatment of blepharitis, conjunctivitis and corneal ulcer. In most of these infections the staphylococcus was considered the infecting organism. Cashell also treated in a similar manner 6 eyes with infected perforating injuries; in 3 of these eyes the response was satisfactory. In most of the aforementioned cases the sodium or the calcium salt of penicillin, in concentrations of from 400 to 1,500 Oxford units per cubic centimeter, was used locally, in the form either of an aqueous solution or of an ointment. Single cases reported by Griffey,[8] Herrell [9] and Barker,[10] in which penicillin was used systematically, may be added to these series.

Although the experimental studies on ocular infections may have encouraged the clinical use of penicillin, they have contributed little to the treatment of surface infections of the eye. However, the successful treatment of experimentally produced, standardized corneal ulcers by Robson and Scott [11] and of standardized intraocular

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2. Florey, M. E., and Florey, H. W.: General and Local Administration of Penicillin, Lancet **1**:387-397 (March 27) 1943.

3. Bodenham, D. C.: Burns of the Eyelid and Conjunctiva, Brit. M. J. **2**:522-523 (Oct. 23) 1943; in Discussion on Burns of the Eyelid and Conjunctiva, Proc. Roy. Soc. Med. **37**:30-32 (Nov.) 1943.

4. Sorsby, A.: Ophthalmia Neonatorum, Brit. M. J. **2**:723 (Dec. 4) 1943.

5. Lyons, C.: Penicillin Therapy of Surgical Infections in the U. S. Army, J. A. M. A. **123**:1007-1018 (Dec. 18) 1943.

6. Berens, C.: Some Clinical Experimental, and Pathological Conditions of Chronic Uveitis, to be published.

7. Cashell, G. W., in Discussion on Burns of the Eyelids and Conjunctiva, Proc. Roy. Soc. Med. **37**:32-33 (Nov.) 1943.

8. Griffey, W. P.: Penicillin in Treatment of Gonorrheal Conjunctivitis: Report of a Case, Arch. Ophth. **31**:162 (Feb.) 1944.

9. Herrell, W. E.; Heilman, D. H., and Williams, H. L.: The Clinical Use of Penicillin, Proc. Staff Meet., Mayo Clin. **17**:609-616 (Dec. 30) 1942.

10. Barker, L. F.: Gradenigo Syndrome Complicated by Pneumococcic Meningitis: Recovery After Intensive Treatment with Penicillin and Sulfadiazine, Am. J. M. Sc. **206**:701-703 (Dec.) 1943.

11. Robson, J. M., and Scott, G. I.: Effect of Certain Chemotherapeutic Agents on Experimental Eye Lesions

(Footnote continued on next page)

infection, with injury to the lens, by one of us (L. von S.) [12] should be a guide to chemotherapeutic procedure with the human subject. Robson and Scott followed Florey's method of frequent instillation, while the experimentally produced intraocular infections were treated by corneal bath and iontophoresis.

Two observations were made consistently in the various experiments: first, the significant superiority of penicillin therapy of ocular infections over treatment with various sulfonamide compounds, and, second, the importance of early treatment to assure the best results. A study on the penetration of penicillin into the eye (von Sallmann and Meyer [13]) disclosed that frequent use of drops or ointments did not produce any detectable antibacterial activity in the aqueous and that the addition of two different wetting agents of the aerosol group (penetrasol B and aerosol B) was without effect. On the other hand, after a single corneal bath moderate inhibitory action of the aqueous was present for from two to three hours. The ionization method secured ten times as great an amount of penicillin in the aqueous, the concentration remaining above the bacteriostatic level for over four hours. It was this observation that suggested the use of these more drastic therapeutic procedures in the experiments on intraocular infections of the anterior segment.

It will be noticed from this brief review of the literature that clinical evidence as to the usefulness of penicillin in infections of the eye is based on experience with a considerable number of cases of blepharitis and conjunctivitis and on a moderate number of cases of benign corneal ulcer and infected corneal wounds. Because treatment of severe infections of the globe with penicillin has not yet been reported on, we present the limited evidence provided by the few cases at Presbyterian Hospital in which this therapy was employed. Before the report of the case histories, it should be emphasized that the effectiveness of treatment with any drug of specific antibacterial action is clearly demonstrated only when the identified organism has been found susceptible to the inhibitory action of that compound by in vitro tests. Great care was therefore exercised in studying these cases bacteriologically and in testing the sensitivity of the organism to inhibition by penicillin.

The cases are divided into instances of infections of metastatic nature and instances of exogenous infections, such as ulcer of the cornea and postoperative or post-traumatic endophthalmitis.

REPORT OF CASES

CASE 1.—A. G., aged 3 years, was admitted to Babies Hospital with acute meningococcic meningitis, type 1, meningococcic septicemia and metastatic meningococcic endophthalmitis of the right eye. The inflammation of the eye was of two days' standing and consisted of severe iritis with hypopyon. No fundus reflex was seen except in a small portion of the upper half of the eyeground. Four iontophoretic applications of penicillin were administered, in addition to intensive systemic medication with sulfadiazine. There was gradual regression of the signs of inflammation, the improvement becoming definite after the second iontophoretic application of penicillin. The opacities in the vitreous were slowly absorbed, but a few were still present at the end of six weeks. The fundus at that time was normal.

CASE 2.—H. M., aged 6 years, was admitted to Babies Hospital with meningococcic meningitis, type 1, meningococcic septicemia and severe metastatic meningococcic endophthalmitis of both eyes. When the patient was first seen, edema of the lid, chemosis and massive purulent exudate in the anterior chamber of the right eye indicated an advanced stage of inflammation; considerable, but fewer, signs were present in the left eye. As treatment, penicillin iontophoresis was given in the right eye and sulfadiazine iontophoresis in the left eye. In addition, extensive systemic treatment with sulfadiazine was used. The response of the more advanced endophthalmitis of the right eye was far more dramatic than the reaction of the left eye. Five days after the onset of therapy the details of the fundus of the right eye were visible, and within eight days the opacities in the vitreous were almost completely absorbed. At this time the vitreous of the left eye was still cloudy. At the end of six weeks the vitreous of both eyes was clear except for a few "floaters." The fundus was normal.

CASE 3.—H. C., aged 28, who was observed by squadron leader A. J. Elliot, had acute gonorrheal urethritis and secondary gonorrheal arthritis, for which he had been treated orally with large doses of sulfadiazine. During the period of this treatment the right eye became inflamed. When the patient was seen nine days later, he showed signs of plastic iritis, the exudate covering the pupil, which was constricted and bound down by posterior synechias. The red fundus reflex could not be seen. Vision was reduced to perception of hand movements at 2 feet (1.2 meters). As treatment, five iontophoretic applications of penicillin were made, supplemented by intravenous injection of 15,000 Oxford units of the substance every three hours for five days. Forty-eight hours after the commencement of penicillin therapy the signs of the iridocyclitis began progressively to diminish, so that on the sixth day vision with cor-

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Produced by Staphylococcus Aureus, Nature, London **149**:581-582 (May 23) 1942; Local Chemotherapy in Experimental Lesions of the Eye, Lancet **1**:100-103 (Jan. 23) 1943; The Production and Treatment of Experimental Pneumococcal Hypopyon Ulcers in the Rabbit, Brit. J. Exper. Path. **24**:50-56 (April) 1943.

12. von Sallmann, L.: Penicillin and Sulfadiazine in the Treatment of Experimental Intraocular Infection with Pneumococcus, Arch. Ophth. **30**:426-436 (Oct.) 1943; Penicillin and Sulfadiazine in the Treatment of Experimental Intraocular Infections with Staphylococcus Aureus and Clostridium Welchi, ibid. **31**:54-63 (Jan.) 1944.

13. von Sallmann, L., and Meyer, K.: Penetration of Penicillin into the Eye, Arch. Ophth. **31**:1-7 (Jan.) 1944.

rection was 20/30. A week later the eye was clinically free from inflammation, and vision with correction was restored to 20/15.

CASE 4.—G. L. M., aged 58, was admitted to the Institute of Ophthalmology with recurrent marginal corneal ulcers. Previous treatment with sulfathiazole and other sulfonamide compounds had brought only temporary relief. At the time of admission a superficial ulcer, 4 mm. wide, extended from 3 to 6 o'clock. Staphylococcus albus, with moderate sensitivity to penicillin, was isolated on culture of material from the ulcer. As treatment, penicillin sodium, in 0.5 per cent concentration, in an ointment base composed of anhydrous wool fat with 10 per cent liquid petrolatum, was applied at three hour intervals, with immediate relief of the symptoms. The ulcer healed in five days.

CASE 5.—C. L. C., aged 68, with diabetes, had a variable blood sugar level of from 100 to 310 mg. per hundred cubic centimeters despite a dietary regimen and treatment with insulin. A modified LaGrange operation for glaucoma was performed on both eyes. Three weeks later a small corneal ulcer was noticed near the limbus at 9 o'clock in the left eye, and the lesion spread during the following three days despite local treatment. On December 5 the ulcer was deep and had a densely infiltrated margin, covering more than the temporal half of the cornea. Hypopyon, the accumulation measuring 2 or 3 mm., was seen. A mannitol-positive strain of Staphylococcus aureus, with average sensitivity to penicillin, was isolated. Because of the apprehension of the patient, iontophoresis could not be employed, but penicillin was introduced by means of corneal baths for one to three minutes daily, supplemented by hourly instillation of the substance for six days. Although the ulcer did not progress nasally, it perforated on December 14, with expulsion of the lens, and the eye was enucleated.

CASE 6.—W. C., aged 6 years, was admitted to the Institute of Ophthalmology because of perforating injury of the cornea with traumatic cataract. The wound, caused by scissors, was located in the temporal half of the cornea. There were moderate signs of inflammation, consisting of ciliary injection of the eye, many cells in the anterior chamber, a small amount of exudate, and the formation of posterior synechias. Treatment consisted of one iontophoretic application of penicillin, supplemented by systemic administration of sulfadiazine. The following day the anterior chamber was clear and the pupil well dilated. The further course was uneventful.

CASE 7.—A. P., aged 73, had an intracapsular extraction of the lens of the right eye on May 26, 1943. Recovery was uneventful, vision with correction being 20/15. There remained over the temporal pillar a small cystic scar, which was covered with a thin layer of conjunctiva. Early in the morning of Dec. 1, 1943 the patient had a sharp pain. He was seen within three hours, at which time there was pronounced ciliary injection with intense photophobia and profuse lacrimation. Examination revealed a small area of denuded conjunctival epithelium at the site of the cystoid cicatrix. The anterior chamber was present, however, and no cells were observed in it. The patient was immediately hospitalized and placed under treatment with applications of an ointment containing 5 per cent sulfadiazine four times a day, and a protective dressing was applied. The next day there was a whitish ulcer at the site of the filtering cicatrix; the aqueous was turbid, and the iris was conspicuously congested. The infection had evidently extended inward, and a diagnosis of beginning endophthalmitis was made. No details of the fundus could be seen, and vision was reduced to perception of light. Culture of material taken at this time revealed numerous colonies of hemolytic Staph. aureus. The mannitol test gave a positive reaction. An iontophoretic treatment with a 0.25 per cent solution of sodium penicillin for three minutes was given daily for the next four days, local therapy being combined with intensive systemic sulfadiazine therapy. The inflammatory signs gradually regressed; the exudates absorbed, and the vitreous cleared to a remarkable degree. At the time of the last examination, on May 8, 1944, vision with correction was 20/40, and, except for stringy opacities in the vitreous, the eye appeared normal.

CASE 8.—W. A. R., aged 72, with diabetes, underwent extracapsular extraction with complete iridectomy on the right eye on Sept. 1, 1943. Operation was uneventful, but at the time of the first dressing, forty-eight hours later, the lids were edematous. There was a profuse conjunctival discharge; the cornea was cloudy, with a beginning ring abscess, and the anterior chamber was full of exudate. Culture of material from the conjunctiva revealed a mannitol-positive Staph. aureus. Iontophoretic treatment with a 0.25 per cent aqueous solution of sodium penicillin for five minutes was repeated for three days, without benefit; so enucleation was performed on September 8. Histologic examination confirmed the diagnosis of panophthalmitis and ring abscess of the cornea. Cultures of the vitreous showed a strain of hemolytic Staph. aureus with a strongly positive mannitol reaction.

CASE 9.—H. R., aged 62, underwent intracapsular extraction with complete iridectomy on the left eye on Nov. 3, 1943. Convalescence was uneventful except for the appearance of a small prolapse of the nasal pillar of the coloboma, which was completely covered with conjunctiva. The patient reported on Jan. 12, 1944 with a history of slight discomfort, and examination revealed a small area of infiltration in the cornea adjacent to the prolapsed area of the iris. Use of an ointment containing 5 per cent sulfathiazole and application of hot compresses were advised. When the patient was next seen, ten days later, there were pronounced ciliary injection, steamy cornea, turbid aqueous, hypopyon, measuring 2 mm., and tension of plus 3. Daily iontophoretic applications of a mixture of 0.25 per cent solution of sodium penicillin and 5 per cent solution of sodium sulfacetimide for the next week brought about gradual lessening of the inflammation. The exudate in the pupillary area became organized, and the cornea lost most of its transparency and became partially vascularized. At present the eye is quiet, but vision is nil.

CASE 10.—S. F., aged 64, had trephination of the left eye for chronic simple glaucoma on Sept. 29, 1943. Recovery was uneventful, with the formation of a somewhat thin, filtering cicatrix. On March 17, 1944 the patient returned, complaining of pain in the left eye of three or four days' duration. Examination revealed an intense conjunctival injection, particularly around the cicatrix, which appeared hazy, giving the impression of purulent content. There was considerable mucopurulent secretion from the conjunctiva. Culture of material revealed Staph. aureus with a strongly positive mannitol reaction. Iontophoretic treatment with a 0.25 per cent solution of sodium penicillin was given for four minutes that day, and a corneal bath with the same solution, for the next two days. An ointment containing penicillin in 0.5 per cent concentration was also used locally every four hours, and large doses of sulfadiazine were given by mouth. Within four days there was complete regression of all the inflammatory signs, and the eye has remained normal up to the time of writing.

COMMENT

It is known that metastatic meningococcic endophthalmitis responds favorably to systemic therapy with the sulfonamide compounds. It is difficult, therefore, to evaluate the effect of local treatment when it is combined with the general systemic administration of sulfadiazine, as in the 2 cases described. Only the spectacular improvement of the advanced ophthalmia in the right eye of the second patient can be attributed to the combined use of sulfadiazine and local penicillin therapy, since the inflammatory signs of the other, less involved, eye regressed more slowly with sodium sulfadiazine iontophoresis. Local treatment with penicillin may have been the effective factor in the case of metastatic gonorrheal endophthalmitis reported by Elliot,[14] although more evidence is necessary to prove this assumption. It may well be that systemic use of sulfonamide compounds or penicillin is the chief therapeutic factor in the treatment of infections due to susceptible organisms entering the eye from the blood stream and invading first the richly vascularized structures of the globe. However, if one may judge from the results obtained in experiments on animals, exogenous infections of the globe seem to respond better to local than to systemic treatment.

The effect of specific antibiotic drugs on ulcer of the cornea should be cautiously evaluated, since the causative role of an organism cannot be assumed from its presence on the surface of the lesion, especially if such an organism is ubiquitous and belongs to the normal flora of the conjunctival sac. In the great majority of the reported cases, including the cases in our series, neither the beneficial response to the therapy nor the failure can be related convincingly to treatment with penicillin. Many more observations are necessary for its evaluation. Similarly, at present no definite answer can be given to the question whether the frequent use of drops or ointments, of varying penicillin content, is effective in treatment of severe corneal infection.

An even greater difficulty exists in establishing the etiologic diagnosis in cases of exogenous intraocular infections. It is common knowledge, however, that such postoperative and post-traumatic inflammatory conditions of bacterial origin are predominantly caused by pyogenic cocci and clostridiums. As most of the strains of these species are highly or moderately susceptible to the bacteriostatic action of penicillin, the differential bacteriologic diagnosis of such infections is of minor importance. The possibility may be considered, however, that in rare instances the infective organism is not susceptible to penicillin but is sensitive to sulfonamide compounds. It is feasible to meet such a situation with the simultaneous introduction of a mixture of the two antibiotic agents. The applicability of this combined treatment was shown in experiments on animals by one of us[15] and was also suggested on the basis of in vitro experiments by Spink and co-workers.[16]

Since high levels of the drug were found in the aqueous after corneal bath or iontophoresis, the latter technic was used in treating intraocular infections in our series with either penicillin alone or with the mixture of sodium sulfacetimide and sodium penicillin. Treatment repeated once daily for one to two weeks caused no signs of damage except for a transient haziness of the cornea. The same method was selected in the case of infection of the vitreous in an aphakic eye because it was assumed that, in the absence of the lens, penicillin could penetrate into the vitreous from the anterior chamber. The improvement of the severe inflammatory signs a few days after the first treatment suggested that the infection was halted by the introduction of penicillin. In case 6, with intraocular infection, the evidence that iontophoretic introduction of penicillin had improved the moderately severe post-traumatic inflammatory process was not so convincing. The failure of the penicillin treatment of the diabetic patient with postoperative staphylococcic endophthalmitis and beginning ring abscess had its parallel in the failure of the therapy with animals in which staphylococcic infections of the anterior segment had been produced experimentally if ring abscess or severe suppuration had developed. The infected bleb which followed the Elliott trephening operation responded satisfactorily to local treatment with penicillin, but such lesions are often helped by other therapeutic procedures.

In conclusion, the effectiveness of treatment with penicillin seems sufficiently established for infections of the lid border and conjunctiva with pyogenic cocci and gonococci. Cases of severe corneal infection and of exogenous intraocular infection of the same bacterial origin are too few to offer one an adequate basis for judging

14. Elliot, A. J.: Gonorrheal Iridocyclitis Treated by Penicillin, Canad. M. A. J. **51**:257-259, 1944.

15. von Sallmann, L.: The Simultaneous Local Application of Penicillin and Sulfacetimide, Arch. Ophth. **32**: 190-192 (Sept.) 1944.

16. Spink, W. W.; Ferris, V., and Vivino, J. J.: Comparative in Vitro Resistance of Staphylococci to Penicillin and Sodium Sulfathiazole, Proc. Soc. Exper. Biol. & Med. **55**:207-210 (March) 1944.

their general response to penicillin therapy. Nevertheless, observations in single cases indicate that the prognosis in such cases with penicillin treatment is apt to be more favorable if the destructive process is not too far advanced.

An even more optimistic outlook arises from the results of experiments with intraocular infections. Since the beneficial results of penicillin iontophoresis in treatment of pneumococcic and staphylococcic infections of the anterior segment have been reported, only the studies on deep infections of the lens and vitreous will be discussed.

The Lens.—It has been shown in previous experiments that the favorable results obtained with penicillin iontophoresis in treatment of staphylococcic and pneumococcic infections of the anterior chamber were not essentially impaired when the lens had been injured at the time of inoculation. In a more recent series the infective organisms were inoculated into the central or the posterior portion of the lens. Treatment, starting at various intervals, consisted of iontophoretic applications of penicillin to the cornea or of direct injections of the drug into the lens.

Results of Iontophoretic Treatment and of Intralenticular Injection with Sodium Penicillin at Two Different Intervals After Inoculation of the Lens with Staph. aureus

Treatment	Hours Between Infection and First Treatment	No. of Eyes	No. of Eyes in Which: Infection Was Checked	No. of Eyes in Which: Infection Was Not Checked
Iontophoresis	6	6	0	6
Intralenticular injection	6	6	6	0
	24	10	2	8
Control eyes, untreated.	..	6	0	6

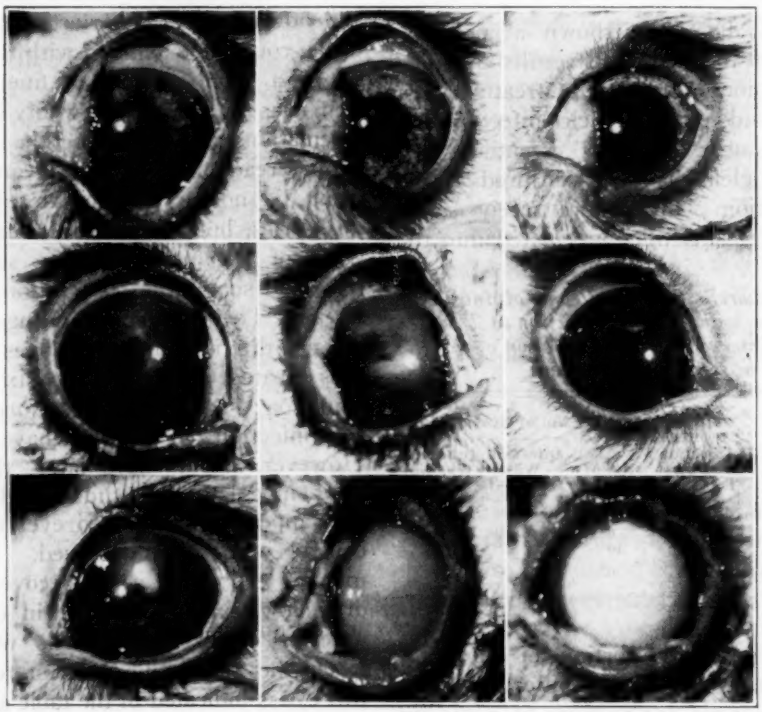
Three hundredths cubic centimeter of a twenty-four hour broth culture of a mannitol-positive strain of Staph. aureus in 10^{-4} dilution was introduced with a fine needle which had pierced the cornea and the anterior portion of the lens above the middle of the pupil. The injection of 0.1 cc. of the penicillin solution was made behind the diaphragm of the iris by inserting the needle 4 mm. posterior to the limbus and observing through the pupil the position of its point in the lens. If massive exudate or cataractous changes prevented visibility of the needle, its correct placement was estimated from its length and the general direction of its insertion. Only one treatment was given in each experiment. The technic of the penicillin iontophoresis was the same as that described in an earlier publication.

The results, consistent for each six hour series, are given in the table. In the iontophoretically treated eyes acute or subacute exudative endophthalmitis septica developed, which finally led to shrinkage of the eyeball. In contrast, the eyes given injections of penicillin six hours after inoculation were saved. Examination with the slit lamp and the ophthalmoscope during the period of observation of seven weeks revealed no signs of damage due to the treatment other than localized opacities in the lens. The infective focus in the treated eyes frequently presented a delicately branched formation resembling a small fir tree, whereas the injection of penicillin produced a localized, translucent, gray area in the posterior cortex. Except for one eye, in which the opacity of the lens was unusually extensive, the details of the fundus were visible and normal. The anterior part of the vitreous, which could be examined with the slit lamp, contained a small number of fine, white deposits. Ten eyes were treated twenty-four hours after inoculation, at which time the signs of inflammatory reaction were well advanced. The treatment did not arrest the infection in 7 eyes of this series, but 2 globes were free from clinical signs of inflammation after several days and remained so for the observation period of seven weeks. The cataractous changes in these eyes did not differ from the changes observed in the eyes treated with penicillin six hours after inoculation; the fundus seemed normal, and the infection seemed to have been checked. However, a few days later, that is, 52 days after inoculation, a sudden, violent inflammation appeared in the two eyes and was beyond control when first observed. Finally, the remaining eye of the series recovered, but an area of yellow exudate, 2 mm. in diameter, in the anterior cortex of the lens was still present when the rabbit died of intercurrent disease; this eye is indicated in the table as lost. Panophthalmitis developed in the control eyes within a few days after inoculation.

Histologic examination of the successfully treated eyes revealed that the signs of inflammation other than those of the lens were limited to the presence of a small number of leukocytes and round cells in front of the disk and in the anterior part of the vitreous. The retina appeared normal. In 2 eyes the lens showed, besides local cataractous changes, a few degenerated leukocytes and cellular debris within a circumscribed area of the posterior cortex. The presence of micro-organisms could not be definitely ascertained in this area. The opacities, which resembled fir trees on observation with the slit lamp, were identified histologically in 2 eyes as masses of cocci, most of them irregularly stained and morphologically changed. There was no leukocytic infiltration at the site of the foci. It is probable, however, that a flare-up of an acute inflammatory process may have been initiated

from these foci at a later date. No remnants of the inflammatory reaction were observed in 2 eyes.

This series of eyes with infections of the lens produced by immediate inoculation of the lens was of twofold interest. First, it showed that penicillin introduced into the aqueous by iontophoresis did not enter the deeper layers of the lens in sufficient concentration to be effective. If one recalls the very small amounts of sulfonamide compounds present in the lens after systemic treatment and various forms of local introduction, one can assume that other drugs of similar molecular size do not readily enter the lens with the usual clinical methods of treatment. It was also demonstrated in old experiments by Schöler and Uhthoff [17] that fluorescein did not diffuse into the lens either from the anterior chamber or from the vitreous. The usefulness of iontophoresis or other means of transcorneal introduction of drugs seems, therefore, to be confined to cases in which the infection has not become established well within the lens or has not progressed into the deeper structures of the eyes. Second, in 4 of 9 eyes in which the inflammatory process was advanced at the beginning of the treatment the process regressed as the result of the therapy, even in 3 eyes in which penicillin was not injected until twenty-four hours after inoculation. This observation demonstrates the usefulness of penicillin as a therapeutic agent despite the presence of alarming clinical signs of inflammation. It should correct the opinions of persons who think of penicillin as primarily of prophylactic value. Earlier observations on pneumococcic infections of the anterior portion of the eye also favor this point of view. The rate of depletion of penicillin in the lens following its intralenticular injection was not actually studied because of the inevitable inaccuracy of the technic available at present. However, it may be postulated that



Effect of penicillin on infections produced by direct injection of Staph. aureus into the lens.

The first horizontal row represents an eye which was treated six hours after inoculation with a single intralenticular injection of sodium penicillin. The first photograph was taken prior to treatment; the second and third photographs were taken two and three weeks later respectively.

The second and third horizontal rows represent a treated and a control eye of another rabbit in which the treated eye was given an injection of penicillin twenty-four hours after inoculation. The first picture was taken prior to treatment; the second and third pictures were taken five days and three weeks later respectively.

17. Schöler, H., and Uhthoff, W.: Das Fluorescein in seiner Bedeutung für den Flussigkeitswechsel des Auges, in Schöler, H.: Jahresbericht der Augenklinik von Prof. H. Schöler im Jahre 1881, Berlin, 1881; abstracted, Jahresb. d. Ophth. **13**:91, 1882. Schöler, H.: Ueber das Fluorescein in seiner Bedeutung für die Erforschung des Flussigkeitswechsels im Auge, Arch. f. Anat. u. Physiol. (Physiol. Abt.), 1882, pp. 120-122; abstracted, Jahresb. d. Ophth. **13**:91, 1882.

compounds which have entered the lens remain there for a long time, since the experiments with fluorescein by Schöler and Uhthoff demonstrated the presence of the dye in the lens for several weeks after injection. The delay in the flare-up of the inflammatory process in the 2 globes which had been treated twenty-four hours after inoculation also suggests a sustained activity of penicillin and its bacteriostatic character. It may be assumed that viable organisms remained in the depths of the lens despite the absence of any clinical signs of inflammation and that a second injection of penicillin would have resulted in a permanent recovery.

The clinical applicability of penicillin treatment of this type seems evident in cases of posttraumatic and postoperative endophthalmitis in which the lens or remnants of the lens are apparently the seat of the infective focus.

The Vitreous.—Because iontophoresis had failed to arrest infections of deeper parts of the lens and infections which had spread from the anterior segment into the vitreous space, intravitreal injection of penicillin solutions was considered as a logical approach to effective treatment of such prognostically unfavorable conditions. This somewhat hazardous undertaking appeared advisable, also, because the study on penetration of penicillin into the eye showed that no antibiotic penicillin activity of the vitreous fluid could be obtained by other local procedures or by systemic introduction. Only by injection, therefore, was it possible to comply with the basic requirement that treatment with any antibiotic drug is effective only when a bacteriostatic concentration reaches the infective focus and remains there for a certain length of time. The low tissue toxicity and the extreme bacteriostatic activity of low concentrations of penicillin removed some of the objections to such an undertaking. Nevertheless, thorough studies of the toxic effect on the delicate structures of this part of the eye were indispensable. In a study of the chemotherapy of infections of the vitreous [18] it was shown that after the injection of 0.2 cc. of a 0.25 per cent solution of penicillin sodium into the vitreous, the concentration remained considerably above the bacteriostatic level for more than twenty-four hours. At that time the average concentration in the vitreous was 4.5 micrograms per cubic centimeter, an amount which is about five times that required to inhibit growth of the test cultures in in vitro tests. After six hours the concentration was about one hundred times the necessary amount. This observation is in agreement with the results for other closed body cavities, such as the pleural cavity, the joint cavity and the spinal canal, and is of particular interest in evaluation of the therapeutic effect of penicillin when injected into the vitreous. In the same paper [18] the authors reported on a study of the effect of a single intravitreal injection of penicillin as compared with the effect of two injections, the second following the first in twenty-four hours. Also, the damage caused by a rather crude preparation of medium potency, similar to the commercial preparation of penicillin, was compared with the damage caused by a purified, high potency fraction. Examinations at regular intervals with the slit lamp and the ophthalmoscope were carried out for a period of several weeks. The pharmacotoxic effect of the injected chemicals on the intraocular capillaries was estimated by determinations of protein in the aqueous three days after the injections. It was found that the protein content of the aqueous after an injection of purified penicillin exceeded only slightly the protein content of the aqueous of the control eyes, which had received the same amount of physiologic solution of sodium chloride. All eyes were enucleated three to five weeks after the injection for histologic examination, in which special staining methods for the ganglion cells, visual cells and nerve fibers were employed. Lesions of the lens, vitreous and retina were discovered. Delicate subcapsular changes of the posterior cortex were seen in 2 of 11 eyes after a single injection of the purified fraction. In the few eyes which had received one injection of the crude preparation the damage was more pronounced. Two injections of either preparation almost always caused some opacification of the posterior cortical layer of the lens. Opacities of the vitreous were fluffy and transient when one injection of a purified preparation of penicillin was given and were more extensive when crude preparations were used. Two injections, the second following the first in twenty-four hours, caused heavy exudation into the vitreous, sometimes with development of the exudate into organized strands. Although a careful search was made for lesions of the retina, in general no toxic action due to a single injection of a purified fraction was seen. Nevertheless, in 4 of 11 eyes localized areas of retinal atrophy, 1 to 2 disk diameters, were present; these areas had obviously been caused by the close proximity of the deposit of penicillin to the surface of the retina during the first six hours after injection.

18. von Sallmann, L.; Meyer, K., and Di Grandi, J.: Experimental Study of Penicillin Treatment of Ectogenous Infection of Vitreous, Arch. Ophth. **32**:179-189 (Sept.) 1944.

At this time examination of frozen and dissected globes showed that injected material, which diffuses slowly within the vitreous jelly, was limited to about a third of the vitreous space. The use of the crude preparation, and especially repeated injections of either preparation, increased the damage and even led to the development of flat retinal detachment of the exudative type. In view of these results, in order to keep the damage at a minimum, it seemed desirable to investigate further the extent to which the dose could be reduced without essential curtailment of the therapeutic effect. However, in consideration of the unfavorable prognosis for ectogenous infections of the vitreous, it may be concluded that a single intravitreal injection of a purified fraction of penicillin can be regarded as a reasonably safe therapeutic procedure. Also, it can be assumed that the relatively greater size of the human vitreous than of the rabbit vitreous will protect to a certain degree the retina and lens from either chemical or mechanical damage, since the point of the needle can be placed at a greater distance from these structures in the human eye than in the rabbit eye.

Because of these observations, a further series of experiments were conducted to determine the efficacy of intravitreal injection of penicillin for an infection of the vitreous produced by inoculation of a mannitol-positive strain of Staph. aureus. One-twentieth cubic centimeter of a twenty-four hour broth culture was usually employed in a dilution of 10^{-5} except in 4 instances, in which a dilution of 10^{-4} was administered.

Treatment in the first series consisted of one or two injections of 0.2 cc. of a 0.25 per cent solution of purified sodium penicillin of high purity and potency (2,500 Oxford units per cubic centimeter of the 0.25 per cent solution). The first injections were made at six, twelve and twenty-four hour intervals after inoculation. In the first eyes two injections were made, supplemented in some instances by corneal iontophoresis on the third day. Afterward, only a single injection was used. In the second series sodium sulfacetimide, 0.2 cc. of a 10 per cent solution, was introduced six hours after inoculation. Control eyes received the same amount of a 0.9 per cent solution of sodium chloride. Regular systematic studies were carried out with the slit lamp and the ophthalmoscope, and cultures of the heart blood were studied in cases of suspected septicemia. All treated and control eyes were examined histologically four to five weeks after inoculation, at which time almost all clinical signs of endophthalmitis had subsided in the successfully treated globes.

In all 20 eyes given injections of penicillin six and twelve hours after inoculation the infection was checked, 10 eyes receiving only a single injection. The treatment did not stop the inflammatory process in any eye when it was started twenty-four hours after inoculation, although a slight beneficial effect was noticeable in some eyes. Injections of sulfacetimide made in 8 eyes six hours after inoculation resulted so uniformly in failure that further experiments were unnecessary.

Although infection was checked in all eyes treated with penicillin six and twelve hours after inoculation, some damage, due either to the infection or to the treatment, occurred. A circumscribed posterior cortical cataract was formed in 3 eyes of the six hour series and in 5 eyes of the twelve hour series, 6 of these 8 eyes having received two injections of penicillin.

Two changes in the vitreous were observed. Fine deposits, of scintillating appearance, diminished during the time of observation and did not interfere with transparency. Clouds of opacity, sometimes dense enough to prevent examination of the fundus during the first few weeks, generally developed into circumscribed opaque masses, which absorbed in the following weeks. Occasionally, however, dense strands, identified as organized remnants of cellular exudate, showed no signs of regression. The number of injections of penicillin had a definite effect on the extent of the opacity, since the second injection greatly increased the inflammatory signs. The interval between the inoculation and the treatment was less important.

Local areas of retinal atrophy, about the size of 1 disk diameter, were noted in a few eyes. Since they were similar to the areas observed after the injection of penicillin without infection, they were probably caused by the proximity of the concentrated solution to the retina. In other eyes, residues of cellular exudate were seen at the sites of atrophy. A flat, localized detachment around the optic nerve in 2 eyes was attributed to the second injection. The uvea was normal, except that in 2 eyes scattered foci were seen in the choroid.

All the control eyes were lost, although the inflammation in some eyes developed gradually, while in others it ran a fulminant course. The extensive destruction noted in the histologic examination of eyes thirty hours after infection indicates one reason for the almost complete failure of penicillin treatment when begun twenty-four hours after inoculation.

The extremely favorable results of penicillin treatment when begun within twelve to thirteen

hours after inoculation were definite: Without exception all eyes were saved. A larger inoculum used in 4 eyes did not change the effect of treatment. A single injection of penicillin was as beneficial as two injections followed by iontophoresis and caused considerably less reaction.

Infections with only one strain of Staph. aureus were studied. However, since most strains of Staph. aureus, Streptococcus haemolyticus and Diplococcus pneumoniae are highly sensitive to the antibacterial activity of penicillin, a large majority of ectogenous infections of the vitreous should respond satisfactorily to early treatment with penicillin. The disappointing results of the injection of sulfacetimide in these experiments are not necessarily conclusive with respect to its effectiveness against infections with other strains. However, the greater inflammatory reaction which it produced suggests that it should be cautiously used.

Injections of Penicillin into the Anterior Chamber.—In addition to the experimental work just described, the reaction produced by the injection of penicillin into the anterior chamber of rabbit eyes was studied in a small series of experiments. Although iontophoresis is a safe procedure for obtaining fairly high concentrations of the compound in the aqueous for several hours, injection of the substance may be considered in emergency cases in which equipment for iontophoresis is not available.

A 0.5 cc. tuberculin syringe containing 0.2 cc. of one of various solutions of penicillin was armed with a 27 gage needle; in rabbits the fine needle must penetrate the cornea at an oblique angle to prevent seeping of fluid after completion of the injection. By repeated withdrawal of aqueous or of the aqueous-penicillin mixture and reinjection of the latter, a uniform dilution of penicillin of about half the concentration of the original solution remains in the anterior chamber. The sodium salts of highly purified penicillin and of a commercial preparation were compared. The purified fraction contained 2,500 Oxford units per cubic centimeter, and the commercial preparation was made up to dilutions containing 2,500 and 5,000 Oxford units per cubic centimeter. Four experiments were made with each preparation.

Fibrinous exudate of varying amounts was seen six hours after injection: It often contained a moderate number of gray, opaque globules, histologically identified as an accumulation of leukocytes. In addition, a small number of minute, crystal-like deposits of metallic luster were seen with the slit lamp on the surface of the iris. When the purified sample or the higher dilution of the commercial product was used, the exudate disappeared in about twenty-four hours, and the crystals, after several days. With the solution of the commercial product containing 5,000 Oxford units per cubic centimeter, the fibrinous exudate was more extensive and remained about three days. No late effects were discovered in the observation period of six weeks.

These experiments indicate that in the rabbit eye injection into the anterior chamber of a solution of sodium penicillin causes only a transient inflammatory reaction of mild degree, which subsides within one to three days, the period depending on the concentration of the dilution used. No definite difference was noted between the effect of the purified fraction and that of a commercial preparation of equal strength. It is probable that the human eye will react similarly to this procedure and that direct injection of penicillin, therefore, may provide a useful method of penicillin therapy when transcorneal introduction by iontophoresis cannot be used.

SUMMARY

1. Experimental infections of the deeper portions of the lens with a mannitol-positive strain of Staph. aureus were not benefited by penicillin iontophoresis.

2. A single intralenticular injection of a solution of penicillin checked such infections regularly when given six hours, and occasionally when given twenty-four hours, after inoculation.

3. Staphylococcic infections of the vitreous were arrested with a single injection of penicillin when administered within twelve hours after inoculation. Treatment failed when a period of twenty-four hours was allowed to elapse between the inoculation and the therapy.

4. Injections of solutions of penicillin into the anterior chamber of rabbits caused transient inflammatory reaction of a moderate degree for twenty-four to seventy-two hours.

Dr. Karl Meyer and Dr. Devorah Khorazo gave assistance and cooperation in this study. Squadron Leader A. J. Elliot permitted the inclusion of his case in this report.

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USE OF ABSORBABLE SUTURES IN CATARACT SURGERY

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The question whether or not to employ sutures in cataract extraction has been debated for many years. Most surgeons of the present day choose to use sutures of some type. Some prefer a suture which approximates only the conjunctival edges; some anchor a small conjunctival flap down to the episcleral tissue, while others actually approximate the severed edges of the cornea and the sclera at the limbus by means of one or more sutures of the single or of the double mattress type.

While surgical silk has proved in general to be satisfactory suture material, there are types of operations in which it is desirable to have a suture material that is absorbable and therefore does not require removal. Cataract extraction is an example. After the lens has been removed, the eye is frequently sensitive to light. The patient is often nervous, apprehensive and hypersensitive and may jump at the least provocation, possibly just at the most critical time during removal of the sutures, while the surgeon has the end of the suture in the forceps. Complications, such as hemorrhage, rupture of the wound, prolapse of the iris and loss of vitreous, have been observed by all surgeons who have had experience in removing cataract sutures, even occasionally by the most skilful. Avoidance of the possibility of such an undesirable event would obviously be an advance in cataract surgery; so a study of materials which are absorbable and which might replace silk was undertaken in 1939 and is still in progress.

From the Research Department of the New York Eye and Ear Infirmary.

Moving pictures showing the use of the sutures described in this paper and the experimental work done on animal eyes were shown at a meeting of the New York Academy of Medicine, Section on Ophthalmology, Dec. 21, 1942, and at the Forty-Seventh Annual Session of the American Academy of Ophthalmology and Otolaryngology, Section on Ophthalmology, Chicago, Oct. 13, 1942. An abstract of the paper, with discussion, was published in the ARCHIVES (Hughes, W. L.: Catgut Sutures in Cataract Extraction, Arch. Ophth. **29**:867 [May] 1943).

Our purpose in this presentation is to call attention to a special fine, plain surgical gut, the advantages of the use of which we believe outweigh its disadvantages, particularly the elimination of all danger of complications incident to the removal of sutures. That this problem is not simply a local one was evident on a recent visit of one of us to a large ophthalmic institute where surgical silk is used routinely. The director of the institute stated that in approximately 10 per cent of cases the anterior chamber was lost as a result of removal of the sutures, on the tenth to the twelfth day.

Fine black silk has been the almost universal choice of most ophthalmic surgeons. Of recent years, the introduction of the atraumatic needle of good quality, with well sharpened point and cutting edges, has been a decided improvement over the employment of the former type of needle, with an eye through which the thread was looped. This newer needle, with the thread swaged into the end, passes smoothly through the dense corneal and scleral tissue without the resistance at its eye which was met with when the eyed needle was used.

The investigation of the material to be used for suture of the edges of the wound in cataract operations received a particular stimulus five years ago (1938) through the occurrence at the New York Eye and Ear Infirmary of 3 cases of hemorrhage into the anterior chamber at the time of, or immediately subsequent to, the removal of sutures. These hemorrhages cleared up with no serious consequences except prolongation of the patient's stay in the hospital. It was realized, however, that it would be advantageous if, by some measure, the risk from this added trauma could be safely eliminated.

PRESENT INVESTIGATION

The various materials tested were compared, first, with surgical silk and then with each other by employing two sutures of different materials in the same eye. As far as possible, exactly similar atraumatic needles were used with the various materials.

It was thought that several features should be incorporated in an ideal suture.

1. The needle should be designed to meet the following qualifications: (*a*) The point should be sharp; (*b*) the edge near the point should be cutting in order to minimize resistance on its being passed through the tissues; (*c*) the cutting edge should make a track sufficiently large for the rest of the needle and the suture to pass through without resistance; (*d*) the shaft should be polished so that it passes without friction through the tissues; (*e*) the end of the needle into which the suture is swaged should not be larger than the rest of the needle, so that there is not resistance at the end of the needle when it is pulled through the tissues; (*f*) the needle should be full curved and 8 to 12 mm. in length, with parallel flattened surfaces on the concave and convex sides from the midpoint of the needle back to near the end to which the suture is attached; (*g*) the steel of which the needle is made should be tempered, so that it maintains its shape back to the portion into which the suture is swaged, and (*h*) the diameter of the needle should be only large enough to retain its shape under the stress used in passing it through the tissues.

2. The suture should meet the following criteria: (*a*) It should be flexible, so that it does not interfere with the delicate maneuvers of the operative procedure; (*b*) it should be of the least diameter consistent with the strength needed to withstand an intraocular pressure of at least 80 mm. of mercury and of sufficient durability to hold the wound firmly together for at least four or five days; (*c*) it should slide through the tissues with a minimum of resistance; (*d*) it should be readily sterilizable or obtainable in a sterilized form in sealed glass tubes; (*e*) its color should be such as to contrast somewhat with the tissues involved for the purposes of identification, but it should have no unabsorbable dye that might be left in the tissues; (*f*) it should not produce any inflammatory reaction, either in the corneal conjunctiva or in the eye in general; (*g*) it should permit its being tied firmly, and the knot should hold firmly as long as the suture remains; (*h*) the capillarity of the suture should not be so great as to favor the introduction of any external infection into the tissues, and (*i*) the material of which the suture is composed should be such as to maintain its strength until all danger of rupture of the wound is past, and the suture should then be absorbed. It is felt that the first four postoperative days are the most important but that the ideal suture should maintain its usefulness for two or three weeks, without tissue reaction. The question of absorbability was regarded as important, since this property would automatically eliminate all complications incident to removal of the suture.

We decided to search for a suture material that would more nearly approximate the aforementioned criteria than the 00000000 black surgical silk we had been accustomed to use. We therefore made contact with several manufacturers of sutures and presented our problem with regard both to the needle and to the suture. We had excellent cooperation and were provided with round and cutting needles of various sizes swaged onto a variety of suture materials, viz., nylon, twisted and braided; plastic material, single strand and braided, 000 surgical gut (catgut), plain and chromic, and 00000 surgical gut, plain and mildly chromicized.

CLINICAL INVESTIGATION

A standard method of closure of the wound was decided on, viz., two sutures of the modified Stallard type. Two double-armed sutures are passed parallel to the limbus through the superficial corneal layers for about 1.5 mm., one on each side of the center of the wound. The suture extends down about one-half the thickness of the cornea and is most easily inserted by means of a small bident [1] for fixation of the cornea, the two teeth of which straddle the limbus midway between the point of entrance and the point of exit of the suture. Another suture is likewise passed on the other side of the center of the wound. These two sutures are laid downward and can be used for traction of the eye downward, if desired, before the incision is made.

The incision is then made and is uncomplicated by the presence of any sutures in or near the line of incision which might be in danger of being cut at the time of the section. Iridotomy or iridectomy (peripheral or complete, as desired) is done and the wound enlarged if necessary. Each end of each suture is passed through the base of the conjunctival flap and then through the episcleral tissue on the distal lip of the wound and is brought out through the distal edge of the conjunctiva. The first double turn of a surgical knot is taken, but of course enough loop is left over the wound so that it may be opened well for delivery of the lens. As soon as the lens is delivered, the suture loop is pulled up slightly; and if any irrigation is necessary, it is carried out. The knot is then pulled up sufficiently to approximate exactly the edges of the wound, but not enough to cause any overriding, and a second knot, to make a true surgical knot, is pulled up tightly against the first. The pillars of the iris are then replaced, and one end of each suture is passed through the edge of the conjunctival flap directly opposite and tied down against the first two knots with two more turns pulled up tightly against the previous knot. In this manner, exact co-

1. Searcy corneal pick.

aptation of the edges of the wound, with a conjunctival flap covering the wound, is obtained.

For the first part of our experimental work, the right-hand suture in each case was of silk, and the left-hand suture was of one of the various substances being tested. At least six tests were made for each substance.

Results.—The clinical results of the tests were as follows:

1. Nylon: No difference could be seen between silk and nylon.

2. Plastic Material, Single Strand: This material was stiffer and more difficult to handle than silk. It caused local tissue reaction, and the stiff cut ends of the suture knot irritated the eye and lid. The material was nonabsorbable.

3. Plastic Material, Braided: This was more flexible than the single strand plastic material, produced less reaction in the tissues and was nonirritating and nonabsorbable.

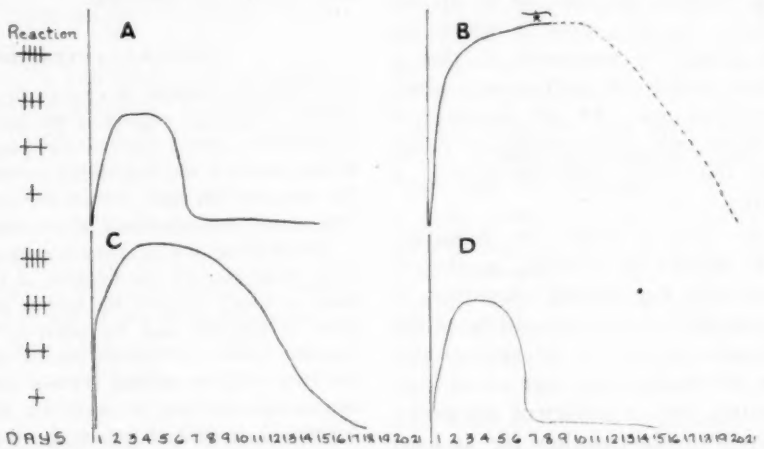

Fig. 1.—Tissue reactions to four types of sutures. *A*, reaction to silk sutures, taken as a standard. As illustrated in the graph, the usual reaction is moderate and continues a few days after removal of the suture. *B*, severe reaction to a solid plastic strand, which lasted several days after removal. R indicates point at which the suture was removed. *C*, reaction to 00000 mildly chromicized surgical gut. *D*, reaction to 00000 plain surgical gut. This was about the same as that to silk.

4. 000 Plain Surgical Gut: The needle and suture were too coarse; the suture was less flexible and produced slightly more corneal reaction than silk. The sutures and needles furnished by two manufacturers were tested. The needles of the one company were of inferior quality with respect to sharpness of point and edges, polish and temper and were irregular at the point at which the suture was swaged on. The sutures were absorbable.

5. 000 Mildly Chromicized Surgical Gut: The needle and suture were too coarse, and the suture was inflexible, even after being soaked in isotonic solution of sodium chloride for some time. This material produced considerably more reaction in the cornea and conjunctiva and in the eye in general than did silk. It was absorbable, but some sutures had to be removed because of local tissue reaction.

6. 00000 Mildly Chromicized Surgical Gut: The needles were of good quality, and the size of the suture was excellent. This material caused considerably more reaction in the cornea and conjunctiva and in the eye in general than did silk. The suture was only moderately flexible. It was absorbable.

7. 00000 Plain Surgical Gut:[2] The needles were of excellent quality, and the size of the suture was excellent. The suture was quite flexible when soaked in saline solution with 5 per cent glycerin for five minutes, although it was less flexible than silk. It caused little tissue reaction, but perhaps slightly more than silk. It produced no local pain or irritation. It was completely absorbed in from five to eight days.

Aside from its absorbability, the last-mentioned material approached silk in all its qualifications, and it was felt that the latter characteristic was a decided advantage. Clinical experience with this suture now extends over a period of four years and includes 200 cases. It was felt that firm support for the wound for four or five days (see experimental data) would be ideal. It has proved to be so by clinical experience. In most of the last 100 cases only the plain 00000 surgical gut suture was used.

Graphs showing the relative reactions (fig. 1 *A* to *D*) and absorption times (fig. 2 *A* and *B*) of some of the types of sutures are presented. At first the reaction of the tissues to silk sutures

2. Manufactured by Davis & Geck, Inc., New York (P322).

was used as a basis. The tissue reaction to 00000 plain surgical gut was approximately the same, or possibly slightly more intense. The reaction to the 00000 mildly chromicized surgical gut was considerably greater than that to silk. In the judging of reactions independent observations were made daily by several members of the staff from the time of the first dressing on the second day after operation.

*Sutures Employed in Experimental Studies**

Surgical gut	00000	P322
Mildly chromicized surgical gut.	00000	1150 (exper. series)
Black braided silk	00000000	P277
White braided silk	000000	P290
Nylon	000000	P336

* Davis & Geck, Inc., furnished all the material used in the animal experiments. All sutures were double armed, swaged on ⅜ inch (9.5 mm.) atraumatic needles with cutting edges.

EXPERIMENTAL WORK WITH ANIMALS

In order to substantiate the clinical results in the use of plain catgut sutures in cataract surgery, we carried out experimental studies on rabbits. In this investigation we noted the absorption process, the tissue reaction, the rate of healing and the resistance to abnormal tension on the wound produced by increased intraocular pressure. As a comparative basis for this study, we employed several types of material. In the table are indicated the sutures used.

Each suture was soaked in 5 per cent glycerin in isotonic solution of sodium chloride prior to use. This rendered the sutures more pliable and facilitated ease of handling. Silk sutures were the most easily handled; chromic surgical gut and single strand nylon offered the greatest difficulty. With the rabbit under anesthesia induced by intravenous injection of procaine hydrochloride, the eye was fixed by application of forceps over the muscle tissue and rotation of the eye into the position necessary. Sutures were placed at 12, 3, 6 and 9 o'clock, by the following method:

The needle was passed through the sclera and 3 mm. of cornea, an attempt being made to maintain the needle in a midcorneal position throughout its course through the tissues. The suture was brought out at this point, and the second stitch was passed through corneal tissue alone at right angles to the first and was again brought out at this point. The third suture was again made at right angles, forming the third side of the square and passing through corneal and scleral tissue. The fourth suture completed the square and was located only in sclera. The suture was tied at this point. The process was carried out in the four quadrants, as mentioned, a different suture being used in each quadrant, so that one section might show all four sutures at the same time.

The sutures were left in position for periods of five, ten, fifteen and twenty days respectively. The eyes removed at these intervals were sectioned for microscopic study. Silk and nylon sutures, of course, showed no absorption whatever. Mildly chromicized surgical gut seldom showed complete absorption in less than thirty-five days. Plain gut sutures could not be distinguished on gross examination after seventeen or eighteen days, and microscopically showed only an area of scar tissue at the end of twenty days.

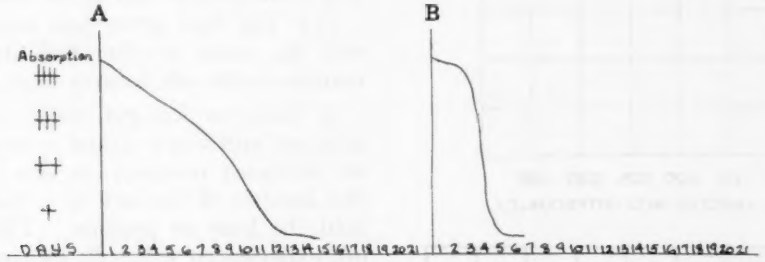

Fig. 2.—Absorption time (*A*) for 00000 mildly chromicized surgical gut, and (*B*) for 00000 plain surgical gut.

The absorbable sutures showed the greatest reaction during the first three or four days after operation, the response becoming less pronounced in later stages. With nylon sutures there was rapid lining of the wound with epithelium-like cells, with a small amount of lymphocytic infiltration about the process. The silk sutures, despite the fact that their channel became lined with epithelium-like cells, produced a rather pronounced lymphocytic infiltration in the surrounding tissue. The tissue reaction was conspicuous over a longer period with the nonabsorbable than with the absorbable sutures. At least four sutures of each type were used, and under otherwise normal conditions absorption and the tissue reaction were uniform.

To evaluate the effectiveness of the different types of sutures in holding the wound closed, we employed the following method:

A series of rabbits were operated on the same day, by a procedure similar to that used in cataract extraction except that the lens was not disturbed. The incision was made with a keratome and enlarged with Stevens scissors to the usual size (two fifths of the

corneal circumference). Sutures similar to those used with patients were employed. Several animals were operated on at the same time, with use of the four types of sutures indicated in the table.

Figure 3 *A* shows the changes in tension of a normal rabbit eye produced by the injection of specific amounts of isotonic solution of sodium chloride into the vitreous, as measured with the Schiøtz tonometer. At the end of each twenty-four hours, one eye was tested by the method just described, and the pressure at which the wound ruptured was ascertained. This method was carried out with all types of sutures. The

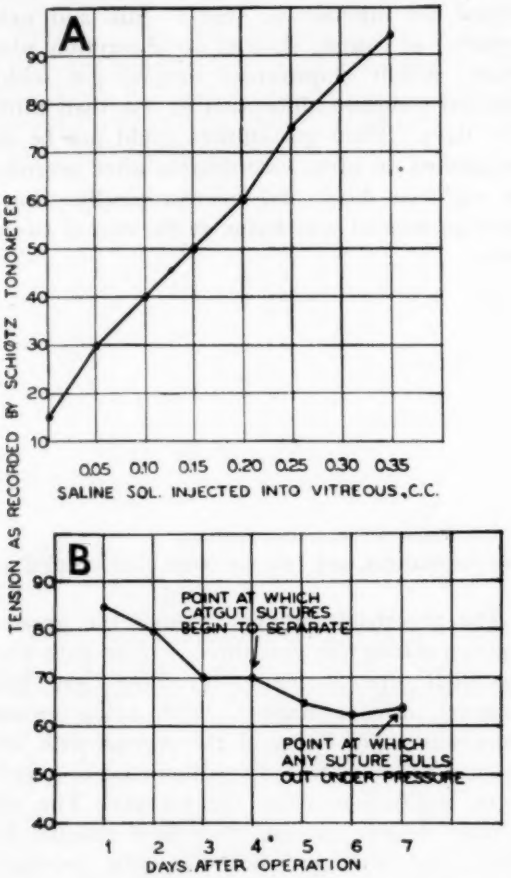

Fig. 3.—*A*, changes in tension in the normal rabbit eye produced by the injection of specific amounts of isotonic solution of sodium chloride into the vitreous. *B*, combined graphs, indicating average points at which the wound ruptured for each postoperative day on which the intraocular pressure was raised by injection of fluid into the vitreous. The time of rupture of the wound was found to be the same with all types of sutures, whether absorbable or nonabsorbable.

second record is a combined graph indicating the average pressure at which a wound ruptures for each day after operation (fig. 3 *B*). This point was approximately the same for all sutures. The points of rupture were in the center of the wound between the sutures or between the sutures and the extremities of the wound. At the end of five days the first sign of weakening in the absorbable sutures was noted. At the end of seven days the absorbable and the nonabsorbable sutures showed a similar tendency to pull through the tissues when put under tension. Healing of the wound progressed at the same rate, regardless of the type of sutures used.

CONCLUSIONS

1. (*a*) The absorbable sutures produced uniformly more tissue reaction in the cornea and conjunctiva, as observed on both gross and microscopic examination, during the first three days after operation than did the nonabsorbable sutures. The 00000 plain surgical gut was completely absorbed at the end of fifteen days, so that the corneal scar became almost invisible when plain catgut was used.

(*b*) With the silk and nylon sutures there was relatively less gross and microscopic tissue reaction during the first five days. The difference was more pronounced at the end of fifteen days.

(*c*) The final gross and microscopic picture was the same whether the absorbable or the nonabsorbable silk sutures were used.

2. Plain surgical gut, mildly chromicized surgical gut and single strand nylon sutures showed an increased tendency to slip after the fourth day because of the lack of a friction element to hold the knot in position. This difficulty was not experienced with silk sutures.

3. Single strand nylon sutures produced irritation in the surrounding tissue because of the stiff, sharp edges of the cut ends.

4. Removal of nonabsorbable sutures from the rabbit eye, even with the animal under anesthesia, was difficult.

5. Plain surgical gut (00000) was adequate to produce more than sufficient support for the wound in cataract extraction and in similar operations involving considerable portions of the limbus in the experimental animal. It was felt that if the wound was firmly supported for five days, the supporting function did not need to be as great subsequently, especially since no sutures of any type held the wound after the fifth to the seventh day but tended to pull out of the tissues.

SUMMARY AND CONCLUSION

An absorbable suture material for use in cataract operations is thought to be more desirable than a material that must be removed, since complications incident to removal of the sutures are automatically avoided.

Fine caliber, 00000 surgical gut was found to be the best size.

Mildly chromicized surgical gut held the edges of the wound about ten to fourteen days but caused objectionable tissue reaction.

Plain surgical gut (00000) caused only slightly greater reaction than silk and held the edges of the wound together about five days.

The knot of the surgical gut suture is too bulky to permit its being tied over the corneal surface. On this account, it is not well adapted to any type of suture in which the knot is tied over rigid corneal tissue.

The ideal suture, holding seven to ten days, colored for ease in identification, economical in price, easy to handle and sterilize and well tolerated by tissues is most nearly approached by 00000 plain surgical gut. This suture is less flexible than silk and is not as ideal from this standpoint. Although we believe that this suture represents an advance, we do not feel that it fulfils all the criteria for an ideal suture.

Various members of the staff at the New York Eye and Ear Infirmary helped in this investigation, and Davis & Geck, Inc., and Bauer & Black furnished the sutures and gave technical advice.

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AMBLYOPIA RESULTING FROM HEMORRHAGE

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Occasionally after profuse distant hemorrhage there is noticed immediately, or, more frequently, after the lapse of days, a sudden diminution of vision, which often goes on to complete and permanent blindness, with the ophthalmoscopic picture of atrophy of the optic nerves. This condition was first described by Hippocrates, and since then excellent clinicians, such as Fries,[1] Moore [2] and Holden,[3] have discussed the subject thoroughly. Many theories as to the pathogenesis of this condition have been offered.

1. Von Graefe [4] specifically assumed that hemorrhage into the optic nerve sheaths was the cause.

2. Westhoff and Ziegler, cited by Theobald,[5] stated the belief that the loss of vision was due to primary fatty degeneration of the optic nerve induced by ischemia.

3. Hoffman, also cited by Theobald,[5] attributed the amblyopia and subsequent atrophy of the optic nerve to retrobulbar neuritis.

4. Leber [6] stated that the ocular changes were produced not only by direct loss of blood but also by retardation of the circulation (stasis [?]) which resulted in edema and multiple hemorrhages in the retina.

5. Goerlitz [7] ascribed the condition to foci of degeneration probably of thrombotic origin, behind the lamina cribrosa.

6. Wolff [8] stated the opinion that this type of amblyopia was due to spasm of the arteries resulting from lack of oxygen. Moore, in discussing Wolff's paper, suggested that the unilaterality observable in some cases indicated a greater tendency to vascular spasm on one side of the body than on the other, such as occurs in migraine.

7. Hartmann and Parfonry,[9] in discussing a case of amblyopia following hemorrhage, reported improvement from almost total blindness to visual acuity of 20/40 in each eye after the use of acetylcholine. They stated that the efficacy of vasodilator therapy indicated that vasoconstriction was the cause of the amblyopia.

8. Groenouw [10] advised that persons who present amblyopia after hemorrhage have previously been ill and that a latent toxin manifests its effect by producing blindiness immediately after the hemorrhage.

9. Holden [3] stated that the process is a peripheral one and that the cause must lie in some product which is formed in the restoration of lost blood which is toxic under certain conditions.

10. Duggan,[11] in his excellent article, stated that the toxin responsible for the amblyopia following hemorrhage is a vasoconstrictor. Epinephrine is most probably the offender. This increased output of epinephrine is due to homeostatic reactions set in action after the hemorrhage. The amblyopia, which often results from closure

From the George Washington University School of Medicine.

Read at the semiannual meeting of the Department of Ophthalmology, George Washington University School of Medicine, Dec. 4, 1943.

1. Fries, S.: Beitrag zur Kenntnis der Amblyopien und Amaurosen nach Blutverlust, Stuttgart, F. Enke, 1876.

2. Moore, R. F.: Four Cases of Serious Loss of Sight as a Result of Hemorrhage, St. Barth. Hosp. Rep. **46**:179, 1911.

3. Holden, W. A.: The Pathology of the Amblyopia Following Profuse Hemorrhage, and of That Following the Ingestion of Methyl Alcohol, with Remarks on the Pathogenesis of Optic-Nerve Atrophy in General, Arch. Ophth. **28**:125, 1899.

4. von Graefe, A.: Sudden and Incurable Amaurosis Following Hematemesis: Report of Cases, Arch. f. Ophth. **7** (pt. 2):143, 1860.

5. Theobald, S.: A Case of Atrophy of the Optic Nerves Following Hemorrhage from the Stomach, with a Consideration of the Causes of Post-Hemorrhagic Blindness, Am. J. Ophth. **16**:145, 1899.

6. Leber, T.: Amaurosis After Hemorrhage, in Graefe, A., and Saemisch, T.: Handbuch der gesammten Augenheilkunde, Leipzig, W. Engelmann, 1877, vol. 5, p. 901.

7. Goerlitz, M.: Blindness Following Severe Loss of Blood: Histologic Study of a Case, Klin. Monatsbl. f. Augenh. **64**:763, 1920.

8. Wolff, E.: The Causation of Amblyopia Following Gastric and Other Hemorrhages, Brit. J. Ophth. **19**:289, 1935.

9. Hartmann, E., and Parfonry, J.: Improvement of Blindness Following Melena After Use of Acetylcholine: Binasal Reduction of Visual Field, Bull. Soc. d'opht. de Paris, February 1934, p. 56.

10. Groenouw: General Diseases of the Eye, in Graefe, A., and Saemisch, T.: Handbuch der gesammten Augenheilkunde, Leipzig, W. Engelmann, 1904, vol. 11, pt. 1, p. 305.

11. Duggan, W. F.: Clinical Vascular Physiology of the Eye, Am. J. Ophth. **26**:354, 1943.

of the central retinal artery, is due to reactions that are physiologic in nature but pathologic in degree. Loss of sight rather than loss of life occurs.

Deprivation of blood to any tissue will, if sufficiently prolonged, cause impairment or loss of function, and if there is any correlation between delicacy of structure and delicacy of function, one would expect that those structures which are concerned with the most delicate functions would be earlier and more readily affected, and thus the delicate retina would suffer before more coarsely constituted and functionary organs. To carry this reasoning a step further, it is not infrequently seen, as a result of pathologic processes, that the optic nerve fibers which emerge from the macular region, the region concerned with direct vision, the acuity of which is many times that of the rest of the retina, are especially vulnerable. In the case to be presented, it was just these fibers which had been picked out, with production of a central scotoma, absolute in each eye.

REPORT OF A CASE

Chief Complaint.—The visual disorder of B. N., a white man aged 22, married, was discovered in a routine examination of university students. When the patient's turn for examination came, he volunteered the information that he could not see straight ahead but could see around the central blindspots and that he had oriented himself to getting along without help.

Vision was 20/200, eccentrically, in each eye. The patient read Jaeger test type I, eccentrically, with each eye, one letter at a time. He could not read words.

Personal History.—The patient had been a normal, full term child and had enjoyed especially good health, having recently passed the examination for aviation cadets. Of the diseases of childhood he had had only measles, and this illness resolved in a normal manner, without complications or sequelae. He had not had any systemic disease or serious injury until the onset of the present illness. He had had two mildly infectious diseases which were irrelevant to the present illness.

Present Illness.—On the night of April 1, 1942 the patient was driving a jeep in maneuvers, when it accidentally overturned, the hub of the front wheels falling in the middle of his chest, crushing it. He lost consciousness and was removed to the hospital. Immediate examination showed that he was breathing stertorously and was in profound shock, with the blood pressure unobtainable. He was incontinent of feces and urine. He was immediately given 250 cc. of plasma, and thirty minutes later he vomited large quantities of blood.

On his regaining consciousness, three days later, his vision was limited to ability to tell the difference between light and darkness. Ocular examination at this time revealed dilated pupils, which reacted sluggishly to light. There were moderately large subconjunctival hemorrhages in both eyes. Both fundi were ischemic, with no discrimination between the vessels, disk and macula. The following day vision began to clear gradually from the temporal sides. As the days wore on, the patient noted clearing areas in the fields of vision, without any uniformity of appearance. Vision improved so slowly that the patient had to be led around. Six months after the accident the fields had cleared sufficiently for the patient to go about without aid, but there was still no central vision.

Ocular Examination (eighteen months after injury).—External Inspection: Right eye: The lids, cilia, conjunctiva, sclera and cornea were normal. The iris was clear. The pupils were larger than normal (about 10 mm.) and reacted to light and in accommodation and consensually. The ocular rotations were normal in speed and amplitude. The tension was 19 mm.

Left eye: The results of examination were the same as those for the right eye. Tension was 19 mm.

Ophthalmoscopic Study: Both disks showed incomplete atrophy, the pallor involving the temporal side. The arteries were constricted and the veins full. Many of the vessels showed evidence of old perivasculitis, and the fundus in general was ischemic.

Refraction: With a —25 D. sphere before the right eye the patient stated that objects appeared clearer. The left eye was emmetropic.

The visual field in both eyes showed an absolute central scotoma, with concentric areas of clear peripheral vision.

COMMENT

Relative Incidence of Etiologic Factors,—Fries,[1] in a careful search of the literature covering the period from 1541 to 1876, found only 106 cases of amblyopia due to hemorrhage. Terson [12] in 1922 reviewed two hundred and fifty publications on the subject. Of Fries's 106 cases of visual disturbance following distant hemorrhage, gastric hemorrhage was the causal factor in 35 per cent; uterine hemorrhage, in 25 per cent; intentional loss of blood, as in venesection or leeching, in 25 per cent; nasal hemorrhage, in 7 per cent; general traumatic hemorrhage, in 5 per cent, and pulmonary hemorrhage, in 3 per cent.

The resulting blindness is usually bilateral, and it may be permanent or transitory. It usually comes in between the third and the seventh day after bleeding but may be delayed for some time. Terson's statistics (1922) are as follows: Blindness occurred during hemorrhage in 8.3 per cent, immediately after hemorrhage in 11.6 per cent, within twelve hours after hemorrhage in 14.2 per cent, within two days after hemorrhage in 19.2 per cent, between three and sixteen days after hemorrhage in 39.2 per cent and later than sixteen days after hemorrhage in 7.5 per cent. In only 10 per cent of cases was one eye alone involved. The age of patients whose cases are recorded ranged from 2 to 77 years.

12. Terson, A.: Pathogenesis of Treatment of Visual Disturbances After Loss of Blood, Ann. d'ocul. **159**: 23, 1922.

Pathologic Picture.—Experiments carried out by Holden [3] on 6 dogs and rabbits at the Pathological Institute of the New York State Hospitals led to the following results, the pathologic observations being, in short: One or two days after a single, profuse hemorrhage, signs of edema of the nerve fiber and ganglion cell layers of the retina were present, and some of the ganglion cells showed evidence of beginning degeneration. Two weeks after a profuse hemorrhage, or after repeated moderate hemorrhages, simple edema of the nerve fiber layer still existing, there were advanced degenerative changes in many of the ganglion cells and in the medullary sheaths of their axis-cylinders throughout the optic nerves, chiasm and tracts.

The ocular changes were so uniform that observations on only 1 animal need be given in detail.

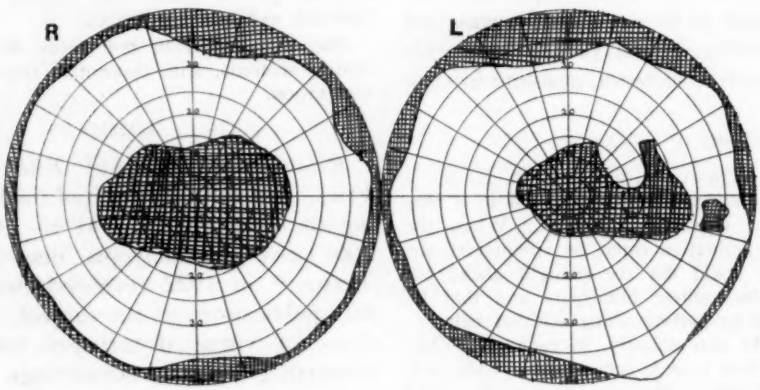
With the animal under narcosis induced with chloroform, 120 cc. of blood was taken from the external jugular vein of a healthy dog, weighing 4.5 Kg., with normal eyes. The animal was killed with chloroform twenty-four hours later, during which period vision apparently was not affected and the ophthalmoscopic picture remained normal.

The retinas, after being fixed in a 5 per cent concentration of solution of formaldehyde U. S. P., hardened in alcohol and cut in paraffin, were stained by Nissl's methylthionine chloride (methylene blue) method and the following changes noted: The fibers in the nerve fiber layer were spaced slightly apart; a number of Müller's fibers were ruptured, and the membrana limitans interna was detached in places—changes indicating the presence of a noncoagulable liquid in the nerve fiber layer, in other words, simple serous edema. Some of the ganglion cells had notched margins, and chromatic granules were absent in the periphery of the cell, this loss indicating beginning primary parenchymatous degeneration. The bipolar cells of the inner nuclear layer, instead of exhibiting a number of granules scattered through the nucleus, contained few granules, and these were arranged mostly just at the margin of the nucleus, an indication of disturbed nutrition of the cell. The retinas were otherwise normal.

The pathologic condition, then, was that of degeneration of a number of retinal ganglion cells, together with their long processes, which make up the centripetal fibers of the optic nerve.

In order to learn whether changes had occurred in other portions of the visual system, the external geniculate bodies, the ganglion cells of the anterior quadrigeminal bodies and the optic radiations were examined for changes in nerve fibers. No notable changes were observed in the ganglion cells of these parts and none at all in the fibers of the optic radiations, an observation showing that in acute general anemia the retinal neurons suffer more than the basal and cortical neurons of the visual system.

Visual Fields.—In patients who have retained vision of an amount sufficient to permit examination of the fields, the results of perimetric study have shown great variations. The narrowing may be slight and concentric, or so great that only a small island remains. Often the field is irregular; it may assume a hemianopsic form, or only one quadrant may be missing. In a case cited by Uhthoff,[13] the nasal half of the field was preserved; the color fields for blue and red were much contracted, and in the blind, temporal half of the retina two small islands were functioning. A normal peripheral field with a central scotoma was observed by Mandelstamm.[14]



Vision was 20/200 in the left eye, eccentrically. There were no central color fields. Stimulus, 25 mm.; illumination, 7 foot candles; distance, 1 meter.

Prognosis.—Amblyopia resulting from distant hemorrhage calls for a guarded prognosis. According to Ball,[15] there seems to be no relation between the amount of blood lost and the degree of possible improvement in vision, nor has the

13. Uhthoff, W.: Optic Nerve Atrophy, Arch. f. Ophth. **26** (pt. 1):275, 1880.

14. Mandelstamm, L.: Etiology of Central Scotoma, Centralbl. f. prakt. Augenh. **3**:178, 1879.

15. Ball, J. M.: Amblyopia from Hemorrhage, Interstate M. J. **20**:531, 1913.

date of appearance of blindness any bearing on the prognosis. Recovery is possible even after perception of light has been abolished for several days provided the pupillary reaction to light is retained. In patients with a more favorable prognosis the amblyopia lasts from a few minutes to many hours.

Groenouw [10] stated that in the majority of patients the improvement—if it comes at all—is noticed, not immediately, but several days, weeks or even months later. He noted that in almost one-half the patient's vision does not improve, in about one-third there is improvement and in about one-fifth central vision is completely restored with defects in the visual field in many cases.

CONCLUSIONS

1. Massive loss of blood from the body may cause serious loss of sight, and, although the patient may recover from the anemia, the blindness is permanent.

2. Evidence afforded by the ophthalmoscope points to thrombosis of the central retinal vein as the usual cause of the blindness that occurs with posthemorrhagic anemia.

3. The blindness is due to degeneration of the ganglion cells of the retina, together with their long processes, which make up the centripetal fibers of the optic nerve. Diminution in size of the vessels is a result, not the cause, of the blindness.

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PARESIS OF RIGHT SUPERIOR OBLIQUE AND OF LEFT SUPERIOR RECTUS MUSCLE

DIFFERENTIAL DIAGNOSIS

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PARESIS OF THE RIGHT SUPERIOR OBLIQUE MUSCLE

Recent Paresis.—In discussion of paresis of the right superior oblique muscle it should be understood that this entity differs in its manifestations, the symptoms depending on whether the paresis is of recent or of late origin. The clinical manifestations vary considerably between the one stage and the other. Also, in the intermediate stage, when the paresis is recovering and the contractures are becoming manifest, the symptoms differ somewhat from those in the early and late stages.

Bielschowsky [1] stated: "By far the most frequent and important type of paralysis of a single vertical motor anomaly is trochlear nerve palsy." This statement is most important because not infrequently there are variations which lead to a wrong diagnosis. Most statistics include too small a number of cases of paresis of the trochlear nerve because they are not recognized.

The most striking sign of this condition is habitual torticollis. This sign is present only when the oblique muscles are involved, either the superior or the inferior; it does not occur when the superior or the inferior rectus muscles are paretic. The two symptoms, torticollis and the upshoot of the eye with the head tipped on one shoulder, constitute the distinguishing feature. Obviously, the patient must be able to achieve binocular single vision. That is, he must have sufficiently good vision in each eye and adequate fusion to appreciate diplopia. The torticollis is invoked by the patient to prevent diplopia. He achieves this by placing the eyes in such a position, by a suitable position of the head, that they will be out of the field of action of the paretic muscle. This explains the habitual position of the head observed in many persons. If the head is turned to the left, the paretic right superior oblique muscle is not called on to function because there is no vertical deviation and the diplopia is relieved.

The ocular origin of torticollis is often not recognized, particularly in cases of congenital trochlear paresis or that acquired in early childhood. The explanation given by Bielschowsky is as follows:

> Wheel-like rotation of the eyes on their antero-posterior axes is due to a reflex innervation of vestibular origin. The parallel rotary movements on the antero-posterior axes can be brought about only by the superior muscles of one eye (the superior oblique and the superior rectus), both of which rotate the eye on its antero-posterior axis to tip the vertical meridian inward, i. e. to the patient's left. At the same time, the inferior muscles, the inferior oblique and the inferior rectus, outward rotators of the other eye, rotate this eye to the left.

Thus, the combined action of the superior muscles, inward rotators of the one eye, and the inferior muscles, outward rotators of the other eye, results in the rotation of both eyes to the left when the head is tipped to the right. When the head is tipped to the left, both eyes are rotated to the right on their anteroposterior axes in a similar manner. This physiologic explanation of the wheel-like rotation of the eyes on their antero-posterior axes is reviewed since it is helpful in understanding (1) the ocular torticollis, (2) the upshoot of the right eye with paresis of the right superior oblique muscle when the head is tipped to the right shoulder and (3) the differential diagnosis of paresis of the right superior oblique muscle and that of the left superior rectus muscle.

The outstanding and diagnostic symptom is the head-tipping test. If the head is tipped to the right shoulder, there is a high upshoot of the right eye (fig. 1).

Bielschowsky explained this diagnostic sign thus:

> If in a case of paresis of the right superior oblique the head is tipped on the right shoulder, there will arise a vestibular excitation of those muscles that produce a parallel rotary movement of both eyes to the left; this movement is produced in the right eye by the superior muscles, the superior oblique and superior

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Read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, Feb. 21, 1944.

1. Bielschowsky, A.: Lectures on Motor Anomalies, Hanover, N. H., Dartmouth College Publications, 1940.

rectus, and in the left eye by the two inferior muscles, the inferior oblique and inferior rectus. The right superior oblique however is paretic and can no longer *compensate* the elevating component of the right inferior oblique and the right superior rectus. Hence, the right eye is turned strongly up and also slightly adducted by these muscles; the head, we remember, is being tipped to the right shoulder.

In this maneuver, the superior muscles of the right eye and the inferior muscles of the left eye receive equal reflex impulses. Since the paretic right superior oblique muscle cannot act, there is overaction of the sound antagonist, the right inferior oblique muscle, and also of its sound agonist (yoke muscle), the left inferior rectus muscle, both these muscles acting under increased stimulus. The diagnostic high upshoot of the

Fig. 1.—Paresis of the right superior oblique muscle. When the head is tilted to the right, there is maximum hyperphoria, with the upshoot of the right eye. There is no vertical deviation with the head tilted to the left.

right eye, however, is the noteworthy symptom. From it one may promptly make a tentative diagnosis of paresis of the right superior oblique muscle. When this sign is coupled with the torticollis, the diagnosis is almost certain.

If the patient's head is tipped on the left shoulder, the vestibular reflex is exerted on the superior muscles of the left eye, the superior oblique and the superior rectus, which tort the left eye inward, i. e., to the right, and this reflex is also exerted on the inferior muscles of the right eye, the inferior oblique and the inferior rectus, which tort the right eye outward, i. e., to the right. Since there is no impulse to the superior muscles of the right eye, the paretic right superior oblique muscle is not called on to act, and hence there is no abnormal deviation of the right eye. Now, one may understand the reason for the torticollis and for the pronounced upshoot of the right eye with the head tipped to the right shoulder when there is paresis of the right superior oblique muscle.

The impression that the torticollis is caused by the patient's tipping his head to lower the higher image was stated by Bielschowsky to be erroneous. He cited as proof of this assertion the observation that if a 10 D. prism is placed base up or base down in front of one eye and the head is tipped alternately to either side, the vertical images will be seen at the same height with respect to the basal line of the eyes. If the head is tipped far enough, the images will appear side by side with reference to the horizon, not one above the other; but they cannot be fused because they are still vertical to the base line of the eyes.

This is illustrated by a drawing (fig. 2) of the images when a 10 D. red prism was placed before the right eye and the head tipped 90 degrees to the right. The base line of the eyes is the line from the nodal point of one eye to the corresponding point of the other eye. When the head is tipped 90 degrees, this line is vertical. The red image is still the higher image in relation to the base line even though the images appear side by side. Obviously, the images are still vertical in relation to the head and eyes; hence, they cannot be fused. This is unequivocal proof that the patient does not tilt his head in order to lower the higher image.

There are other components of the symptom complex resulting from recent paresis of the right superior oblique muscle, though the vertical deviation with the patient's head tipped to the side of the paretic eye, as just described, is the most important.

When the patient is looking down and to the left with the head straight, there is the greatest vertical deviation, since the right superior oblique muscle is in the field of its major action as a depressor of the right eye. Since it cannot act, being paretic, the left eye turns down with increased action, since it is in the field of action of the left inferior rectus muscle, the agonist (yoke muscle) of the right superior oblique muscle. Thus, there is a downshoot of the left eye, as illustrated in figure 3.

When the eyes are turned to the left or up and to the left, there is a high upshoot of the right eye, due to overaction of the right inferior oblique, the antagonist of the right superior oblique muscle. With the eyes turned to the right, however, there is no vertical deviation of the eyes, since the right eye is out of the field of action of the right superior oblique and in the fields of action of the right superior rectus and the right inferior rectus muscle. In this position, however, the right superior oblique muscle acts to rotate the vertical meridian inward. Hence, in the rotation of the eyes to the right there occurs little, or no, vertical deviation, but there is a maximum obliquity of the double images (fig. 4). This is due to the unopposed action of the inferior oblique muscle acting as an extorter with the eyes in this position (looking to the right), i. e., rotating the right eye outward on its anteroposterior axis and hence tipping the verti-

cal axis of the eye outward, or to the right. The *Visierzeichen* is an apparatus devised for making this test. The after-image test may also be used. It should be observed that the diplopia and the obliquity of the vertical meridians are diagnostic signs of value only in cases of recent paresis. One rarely sees such cases, except those of traumatic paralyses, which this paper does not discuss. The important and useful diagnostic

Fig. 3.—Paresis of the right superior oblique muscle, showing overaction of the left inferior rectus muscle, the agonist (yoke muscle) of the right superior oblique.

sign is the objective one, the high upshoot of the right eye on the patient's tipping the head to the right shoulder.

Positions of the Head.—The head is so adjusted that the eyes are in a position to avoid diplopia. To attain this, frequently the head is turned toward the sound side, that is, to the left in case of paresis of the right superior oblique muscle. This turns the right eye out, or abducts it, which takes it out of the field of the paretic muscle so far as the vertical diplopia is concerned. It will be remembered, however, that in

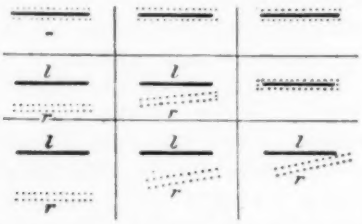

Fig. 4.—Double images (*r* and *l*) of a horizontal object in the various parts of the field of fixation, in a case of palsy of the right trochlear nerve. From Bielschowsky,[1] figure 32.

this position the meridional disclination (rotation of the eyes on their anteroposterior axes) is at the maximum. In order to avoid this form of diplopia, which is disturbing, particularly in reading, causing the lines on the page to cross each other at acute angles, the patient depresses the head and rotates it to the left. This unburdens the right superior oblique muscle completely. There is thus no vertical diplopia and no disclination. Less usual positions of the head are bending the head forward, with the chin against the chest, and turning the head slightly to the left (the sound side) in cases of slight paresis. These positions of the head are so suggestive that one may suspect paresis of an oblique muscle when the patient enters the consultation room.

It is interesting to note why the deviation due to paresis of the vertically acting muscles does not become concomitant, as does paresis of the abducens nerve, for example. The influence of vertically acting muscles varies according to the position of the eyes. When the eye is abducted (turned out), it is within the field of the vertically acting rectus muscles; when the eye is adducted (turned in), it is within the field of the oblique muscles. I know of nothing more helpful than to remember this obvious fact. It will save one a great deal of mental confusion in the diagnosis of the vertical motor anomalies.

Thus, it is apparent that the deviation due to paresis of a vertically acting muscle cannot become concomitant in the ordinary sense, since the deviation occurs only in the field of action of the oblique or the vertical rectus muscles. Consequently, it can be concomitant in these fields only.

The secondary deviations continue in cases of long-standing paresis after the recovery of the paretic muscle. Hence, in a study of the deviations of the vertically acting muscles, the diagnosis should be quite clear as to whether the paresis is recent or is old and is no longer the outstanding feature. In such cases study of secondary deviations gives the diagnostic data.

One rarely sees cases of recent paresis of the vertically acting muscles, principally because they occur largely among children, who are too young to be studied with sufficient accuracy to permit an assured diagnosis. One must reiterate for emphasis: The diagnosis in the vast majority of the cases of paresis of the vertically acting muscles rests on the overaction of the agonist and the antagonist of the paretic muscle. It therefore becomes difficult in cases of late paresis to differentiate between the paresis of a vertical rectus and that of an oblique muscle. Recent paresis of the right superior oblique muscle has been considered; a case of late paresis of this muscle, in which only the agonist and the antagonist were overacting, will now be discussed.

Late, or Old, Paresis.—In this condition there is no lag of the right eye when the patient looks down and to the left, as there is in a case of recent paresis of the right superior oblique muscle.

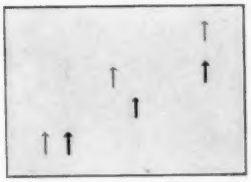

Fig. 2.—The red arrows indicate the right image; the black arrows, the left image, when a 10 D. prism base up or base down is placed before the right eye. Vertical images are seen at the same height with respect to the basal line of the eyes. The images cannot be fused with the prisms in any position.

Since my associates and I have studied the motion pictures of this condition, we have become acutely aware of the overaction of the two muscles (the agonist and the antagonist). The antagonist overacts much more than the agonist (yoke muscle): When the eyes are turned up and to the left, the antagonist of the right superior oblique muscle, which is the right inferior oblique, overacts energetically, and there is the familiar upshoot of the right eye. When the eyes are turned down and to the left, the agonist (yoke muscle), which is the left inferior rectus muscle, overacts, but to a lesser extent than the right inferior oblique, the antagonist, and there is a downshoot of the left eye. Until we studied the slow motion pictures we did not fully appreciate this fact.

Secondary contracture of the antagonist, the right inferior oblique muscle, gradually, occurs; this causes right hyperphoria, which varies little in degree on the patient's looking up or down. This condition differs from that associated with recent paresis, in which there is a higher degree of hyperphoria when the patient is looking down and to the left, since the right eye does not turn down, owing to the paretic right superior oblique muscle, while there is a downshoot of the left eye, as a result of overaction of the left inferior rectus muscle. In a case of recent paresis this downshoot really creates a left hypophoria, which, added to the lag of the right eye when the eyes are turned down and to the left, causes a high degree of right hyperphoria. In a case of late paresis there is no lag of the right eye, since the paretic right superior oblique muscle has recovered, but there remains when the eyes are turned down and to the left only the overaction of the yoke muscle, the left inferior rectus, producing the downshoot of the left eye, which is called right hyperphoria but is in reality left hypophoria. With the eyes looking toward the left, there is right hyperphoria, due to overaction of the right inferior oblique muscle. This does not change in degree when the eyes are looking up or down since it is due to contracture of the right inferior oblique. It must be borne in mind that late paresis of the right superior oblique muscle is under consideration. Hence, the difference in the vertical deviation is greater in the lateral movements of the eye than in the vertical movements. This is quite different from the deviation in a case of recent paresis, in which the vertical deviation is greater in the vertical movements. As noted before, in the cases of late paresis of the right superior oblique muscle, the other symptoms are of no moment, i. e., disclination of the vertical axes as manifested by the after-image test and by the apparatus designed by Bielschowsky on the principle of Helmholz' *Visierzeichen.*

When the eyes are turned to the right, up and to the right or down and to the right, there is no vertical deviation; since the right eye is abducted, the right superior oblique muscle has no power to move the eyes vertically. In this position it has only the power of torting the eye, which is noted on the chart in figure 4. When the eyes are turned in the opposite direction, that is, to the left, only the vertical deviation is seen. The right eye being adducted, the right superior oblique muscle is in the position of maximum power as a vertically acting muscle. Hence, with the eyes turned down and to the left the greatest vertical deviation is observed. This is to be observed only in cases of recent paresis, be it remembered. It has little value in cases of the late stage. To recapitulate, one rarely sees a case of recent paresis of the superior oblique; at least this is true in our experience. Thus, again, it is obvious that the head-tipping test is the main reliance in differential diagnosis, which may be important from the point of therapy.

Hence, it becomes evident that a differential diagnosis of paresis of the right superior oblique and paresis of the left superior rectus muscle is of importance. The symptoms are much the same in cases of the late stage, since the meridional deviations cannot, in most cases, be demonstrated either with the aforementioned instrument or by means of the retinal after-images. This is assumed to be due to suppression, which develops early in children. Since practically all cases of paresis are seen in young children, the condition occurring either congenitally or having its inception early in infancy, suppression has taken place before the child is mentally mature enough to be examined with such appliances.

Summary.—1. In cases of recent paresis of the right superior oblique muscle, the most important diagnostic symptom is the wide vertical deviation, or high hyperphoria, when the head is tipped on the right shoulder. This is true also in cases of late paresis.

2. Meridional deviations are less valuable, for the reasons stated.

3. Since the superior oblique muscle is in slight degree an abductor, there is slight esotropia or esophoria when this muscle is paretic. With paresis of the left superior rectus muscle there is slight exotropia or exophoria. These lateral deviations are uncertain, slight or perhaps absent and, in consequence, are of little value in the differential diagnosis.

Therapy.—Correction of the vertical deviation is necessary and should be accomplished as

early as possible in the life of the child. This is of paramount importance, for the following reasons: 1. The torticollis is disfiguring and in time produces spastic contractures of the muscles of the neck, head and trunk. 2. Skeletal deformity may result from the unbalanced weight of the body as a result of the head's being held on one side. 3. Suppression and amblyopia may occur in the paretic right eye. 4. If suppression and amblyopia develop, the right eye will remain deviated upward, and this becomes a serious factor in the child's appearance, a real deformity, the psychologic, social and economic importance of which cannot be overestimated. If suppression occurs, it is obvious there will be no torticollis.

Therapy is surgical; orthoptic training is indicated when the deformity has been surgically corrected. The first essential is a correct diagnosis; otherwise, irreparable harm may be done.

With dissociated hyperphoria any surgical procedure is particularly to be avoided; in some cases this form may closely resemble the hypertropia of paresis of the superior oblique muscle, treatment of which is purely surgical. To confuse the diagnosis of these two forms of hypertropia may be fatal to binocular single vision. The higher degrees of hypertropia, esotropia and exotropia are likely to be complicated by dissociated hypertropia.

The surgeon should strive for binocular single vision, and not merely a cosmetic effect, important as it is. If he stops here, however, he has not restored function. This is not the time or place to discuss the necessity of binocular single vision. Its value in later life is great, and the lack of it is a serious handicap.

The usual operation is myectomy of the right inferior oblique muscle. The result is not always satisfactory. In some cases overcorrection occurs; in others there is insufficient correction. The correction is usually only cosmetic, and often is not perfect enough to enable the patient to secure binocular single vision without the use of prism glasses for correction of the remaining hyperphoria. This will be a handicap to the child throughout life and should not become necessary if the surgeon can prevent it. In performing this operation, he makes another paretic muscle, and this is repugnant to his surgical estheticism. When the operation is done, the incision is made through the conjunctiva, and not through the skin. A cutaneous incision is inexcusable. It adds a scar on the face to what is already a sad situation. The conjunctival incision makes the operation more difficult, but what of that? A little practice in the dissecting room overcomes this.

Recession of the inferior oblique muscle from its insertion on the globe is theoretically much more desirable since it modifies the action of this muscle without paralyzing it, as does myectomy. It is a more formidable operation, but this should not enter into the solution of the problem if it will accomplish the desired end.

PARESIS OF THE LEFT SUPERIOR RECTUS MUSCLE

Isolated paresis of the superior rectus muscle in the majority of cases is of congenital origin and frequently is combined with ptosis of the upper eyelid. In many cases the condition is diagnosed as paresis of this muscle which in reality is paresis of the opposite superior oblique muscle. This possible error was commented on by Bielschowsky [1] with some emphasis. Our experience is in agreement with his in that of 88 cases of paresis of the superior oblique and superior rectus muscles in our private clinic, the superior oblique was involved in 48, or 54.5 per cent, and the superior rectus in 40, or 45.5 per cent.

The confusion is brought about by the fact that the symptoms are much the same as those associated with paresis of an oblique muscle. Unless the case is accurately and carefully studied, such an error is likely. With paresis of the left superior rectus muscle, on the patient's looking up and to the left, there is a high degree of right hyperphoria. The same result is noted when there is paresis of the right superior oblique muscle. In the case of recent paresis of the left superior rectus muscle, the right hyperphoria is caused by the following factors: (1) lag of the left eye, which is in the major field of action of this muscle; (2) overaction of the right inferior oblique, the agonist (yoke muscle) of the left superior rectus, and (3) overaction of the left inferior rectus, the antagonist of the left superior rectus.

In a case of recent paresis of the right superior oblique muscle there is the same high degree of right hyperphoria with the eyes looking up and to the left, which is due to the following factors: (1) overaction of the right inferior oblique, the antagonist of the right superior oblique, and (2) overaction of the left inferior rectus, the agonist (yoke muscle) of the right superior oblique.

It should be remembered that when the eyes are abducted, they are in the fields of action of the superior and inferior rectus muscles; when the eyes are adducted, they are in the fields of action of the superior and inferior oblique muscles. One may say that this obvious fact is the key to the situation of the present study. If the

examiner steadily keeps it in mind, he will avoid much mental confusion.

Recent Paresis.—With the eyes in the primary position there will be a right hyperphoria of variable degree; it is likely to be greater in degree for distance than for near vision. The reason for this is that in looking at near objects the right eye is convergent, i. e., adducted, and

Fig. 5.—(*A*) The two eyes are moved up and to the right to an equal degree. (*B*) When the patient is looking up and to the left, the visual line cannot be raised above the horizontal plane. (*C*) When the subject is looking up, the left eye lags behind. (*D*) When the right eye is looking straight ahead, the left eye is deviated downward. From Bielschowsky,[1] figure 38.

This figure is printed in reverse, to show paralysis of the left superior rectus muscle, instead of the right, as shown in the original figure.

consequently more out of the field of the left superior rectus, the paretic, muscle. In looking at a distance with the eyes in the primary position, the left eye will deviate downward, owing to overaction of the left inferior rectus, the antagonist of the left superior rectus. In the position of eyes left, the right hyperphoria is increased, since when the left eye is abducted it is in the field of action of the paretic left superior rectus muscle (fig. 5). The left eye is not elevated above the horizontal plane; likewise, the upshoot of the adducted right eye is in the field of the overacting right inferior oblique muscle.

Fig. 6.—Paresis of the left superior rectus muscle, showing overaction of the left inferior rectus muscle, the antagonist of the paretic left superior muscle.

When the eyes are turned up and to the left, there is the maximum right hyperphoria, due to (1) lag of the left eye, which is greatest with the eyes in this position; (2) overaction of the right inferior oblique, the agonist (yoke muscle) of the left superior rectus, which causes an upshoot of the right eye when it is adducted, as it is in the position of eyes left, and (3) overaction of the left inferior rectus, the antagonist of the left superior rectus. This is usually of lesser degree than is the overaction of the agonist (yoke muscle).

When eyes are looking down and to the left, the left eye is out of the field of action of the left superior rectus, but the overacting left inferior rectus causes a downshoot of the abducted left eye (fig. 6). There is right hyperphoria with the eyes in this position, but usually of lesser degree than when the eyes are looking up and to the left. When the eyes look down and to the left, only the overaction of the left inferior rectus muscle is operative, while with the eyes looking up and to the left two factors operate to make a high right hyperphoria: (1) the lag of the left eye, due to the paretic left superior rectus and (2) the overaction of the right inferior oblique, the agonist (yoke muscle) of the left superior rectus.

The position of the double images in a case of paresis of the left superior rectus muscle is

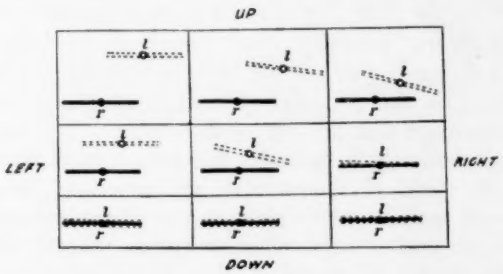

Fig. 7.—Double images of a horizontal object in a case of paralysis of the left superior rectus muscle. From Bielschowsky, figure 37.

shown in figure 7 (Bielschowsky's figure 37[1]). When the eyes are turned up and to the left, there is the greatest vertical separation, together with an esophoria. It will be noted there is no torsion. The esophoria is of no particular moment in the diagnosis, since it is of low degree and may be influenced by an esophoria or exophoria of other origin.

It will be observed that with the eyes looking down and to the left there is no diplopia, an indication that in this case there was no overaction of the left inferior rectus muscle, the antagonist of the paretic left superior rectus muscle. It is to be noted that as the eyes are turned from the left to the right and thus the left eye changes from abduction to adduction, the left eye is in the field of the paretic left superior rectus muscle, acting not as an elevator, but as an intorter; i. e., the vertical meridian is typed inward, or to the right, which means that the horizontal meridian is depressed at its inner end. Since the left superior rectus muscle is now paretic, the inferior rectus muscle acts unopposed

as an extorter, the left eye being in adduction. Hence, the left eye is now extorted, instead of intorted, as shown by the double images. Since the outer end of the horizontal meridian is tipped down, the image appears to be tipped up at its outer end.

Position of the Head: The head is turned toward the paretic, or left side, to bring the eye into adduction and, hence, out of the field of the elevating action of the left superior rectus muscle. The head may also be tilted backward, so that the left eye is turned down. The position of the head may be determined by the intensity of the paresis. When the left eye is adducted, there occurs meridional tipping, so that the lines in reading are doubled, the false image being at an acute angle to the true, or horizontal, image. In other words, a cyclophoria is produced. If the head is tilted sufficiently far back so that the left superior rectus muscle is entirely out of its field of action, no cyclophoria, and of course no vertical divergence, will be present.

Late, or Old, Paresis.—The cyclophoria soon disappears, probably from suppression; hence, as a diagnostic sign it has little or no value. The test with the *Visierzeichen* apparatus and the after-image test are not of assistance. The vertical deviation gradually becomes concomitant in the field of the paretic left superior rectus muscle and in the fields of the right inferior oblique and the left inferior rectus muscle, the

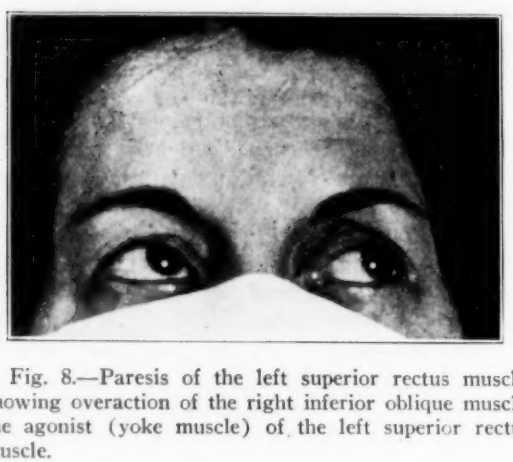

Fig. 8.—Paresis of the left superior rectus muscle, showing overaction of the right inferior oblique muscle, the agonist (yoke muscle) of the left superior rectus muscle.

antagonist of the paretic left superior rectus muscle.

Hence, when the eyes are turned to the left, there is a high degree of right hyperphoria, which does not vary a great deal whether the eyes are looking up and to the left or down to the left, since the deviation due to the paresis is concomitant in this field (fig. 8). Obviously, it can be so only in this field, since there is no displacement of the images of any moment out of this field.

"The head tilting test does not give such unequivocal clues for the diagnosis as it does in paresis of the oblique muscles" stated Bielschowsky.[1] This means that when the head is tipped to the right shoulder and, again, to the left shoulder in a case of paresis of the left superior rectus muscle, there is no high upshoot of either

Fig. 9.—With the head tilted to the right and to the left in a case of paresis of the left superior rectus muscle, no upshoot of either eye occurs.

eye (fig. 9). When, however, the head is tipped to the right shoulder in a case of paresis of the right superior oblique muscle, there is a high upshoot of the right eye, as seen in figure 1. This difference between the paresis of an oblique muscle and the paresis of a vertical rectus muscle is so great and so graphic in moving pictures that when once seen it is unmistakable.

DISCUSSION

Dr. James W. Smith, New York: Bielschowsky, in his eighth lecture, assumed that "by far the most frequent and important type of paralysis of a single vertical motor anomaly is trochlear nerve palsy." He reported that he saw 80 cases in nine years, in 45 of which recovery was spontaneous. I doubt whether I have had 50 cases in twenty-five years of active experience with muscle palsies, and I encounter palsy of the trochlear nerve less frequently than any other type.

Dr. Davis said that the ocular origin of torticollis is not often recognized. My colleagues and I at the New York Post-Graduate Medical School and Hospital are conscious of head tilting and torticollis due to ocular imbalance and are always on the lookout for this clinical sign. Habitual torticollis is seen not only with involvement of the oblique muscles; it occurs often as a sign of underaction of the superior rectus muscle. Bielschowsky, in describing isolated paresis of the superior rectus muscle, in his ninth lecture, stated:

. . . A habitual position of the head will be met with if it helps the patient to see single. The head is either tilted backward or turned to the paretic side, so that the paretic eye is either turned down or in while

an object straight ahead is looked at. Which of these positions is chosen by the patient depends on the intensity of the paresis.

Dr. Davis admitted that he experienced difficulty in the differential diagnosis of old paresis of the right superior oblique and that of the left superior rectus muscle. The symptoms, he stated, were the same in cases of late paresis, since the meridional deviations cannot be demonstrated by either of the Bielschowsky tests. We are able, by means of the screen cover test with prisms and the screen comitance test to make a differential diagnosis even with children 2½ to 3 years old, unless the child is unusually uncooperative. From Dr. Davis' comments on therapy, one might infer that torticollis and skeletal deformities are defects seen only as a complication of paresis of the superior oblique muscle. These defects occur commonly and to a marked degree in patients with untreated paralysis of the superior rectus muscle. In none of the cases of paresis of the superior rectus muscle did amblyopia develop. According to Dr. Davis, the usual operation is myectomy of the right inferior oblique muscle. It is pertinent that Bielschowsky, in his lecture on treatment, mentioned cases of congenital anomalies which he described as overaction of the inferior oblique muscles because evidence of primary paralysis of the trochlear nerve was lacking. He refused even here to consider the diagnosis of congenital paralysis of the superior rectus muscle in the second eye. He also recommended myectomy of the inferior oblique muscle in his cases of so-called congenital overaction of the inferior oblique muscle. My associates and I now employ recession or partial incomplete tenotomy of the inferior oblique muscle as a routine, as in this way we can gage the amount of muscle weakness we wish to induce. The conjunctival incision near the external rectus muscle makes this muscle accessible for resection or recession if the necessary correction of esophoria or exophoria is sufficient to warrant this.

In my clinic at the Hospital for Joint Diseases my associates and I see many cases of deformities of the bones and joints, and we have developed an orthopedic approach to an ophthalmologic problem. Such diagnostic aids as tilting of the head, spasm of the sternocleidomastoid muscle, difference in level of the ears, shoulders and extended fingers and curvature of the vertebral column are often overlooked. When an assistant presents a child for diagnosis, our only test is palpation of both sternocleidomastoid muscles. The patient is then turned about and instructed to walk across the clinic about 15 feet (4.5 meters) to face a brightly colored vertical line on a bare wall. With the patient's inhibitions freed, the diagnostic points stand out in bold relief. To demonstrate the points beyond question, the child is stripped to the waist. If one follows the new instructional feature "Examine the back first and the movements of the eye last," the vertical element in strabismus will never be overlooked.

I have devised a graph of small white squares on a black background for such patients which promises to afford some interesting data on the relation of the degree of head tilting to the amount of hyperphoria. The next step is to compare the angles by means of a protractor, with the ocular deviations measured in prism diopters.

Details of these, and other, tests and of a head rest that has been specially constructed for these patients will appear in a paper now in preparation.

Dr. James W. White, New York: When I first worked with Duane, in 1914, he and Bielschowsky were discussing this matter by letter, and I was in the midst of it. Bielschowsky never convinced Duane, and Duane never convinced Bielschowsky. Dr. Davis has not convinced me, and I shall not try to convince Dr. Davis.

Dr. William Thornwall Davis, Washington, D. C.: Dr. Smith has had a rich experience in anomalies of the oculomotor apparatus. Obviously, what I said regarding the nonrecognition of torticollis due to ocular imbalance does not apply to his associates at his clinic or to himself. Unfortunately, the experience of my associates and myself does not coincide with that of Dr. Smith and his colleagues; we have not seen tilting of the head in cases of paresis of the vertically acting rectus muscles. The patient assumes a position of the head to avoid diplopia, but it is not a tilting to one shoulder or the other. In cases of paresis of the oblique muscles, however, the head is tilted to one side or the other, as is so beautifully shown in Dr. Smith's photographs of paresis of the oblique muscles.

One cannot but wonder whether, in the wide experience that Dr. Smith has had, a condition diagnosed as paresis of a vertically acting rectus muscle may not have been paresis of an oblique muscle in some cases. Our experience coincides with that of Bielschowsky in having observed a higher percentage of cases of paresis of the oblique muscles than of paresis of the vertically acting rectus muscles. Of 88 cases of paresis of the superior oblique and the superior rectus muscle seen in our private clinic, the superior oblique was involved in 48, or 54.5 per cent, and the superior rectus, in 40, or 45.5 per cent. We, of course, use the cover or screen test with children 2 years of age or under. I referred in my paper to our inability to determine the torsion in young children by means of the *Visierzeichen,* or the afterimage, test. These tests are, in our experience, inapplicable in cases of late paresis of the oblique or the vertically acting rectus muscles. This deprives us of important data which could be of value in the differential diagnosis. I regret that Dr. Smith did not discuss further the methods he uses to distinguish paresis of the oblique

muscles from that of the vertically acting rectus muscles. Apparently, he does not accept head tilting as a differential diagnostic sign, or the position of the eyes when the head is tilted to the right shoulder in a case of paresis of the right superior oblique muscle or to the left shoulder in a case of paresis of the right inferior oblique muscle. Since the obliquity of the horizontal meridians of the eyes cannot be determined in cases of the late paresis under discussion, it would be most helpful if he had stated on the basis of what signs, symptoms and tests he makes the differential diagnosis.

Since I was considering paresis of the oblique muscles, the torticollis was discussed only from that standpoint. Since Dr. Smith did not describe his methods of differential diagnosis, but only stated categorically that he has seen torticollis result from paresis of the vertically acting rectus muscles, it cannot but leave me doubtful whether he, like so many others, misses this differential diagnosis on occasion.

Dr. Smith stated: "In none of the cases of paresis of the superior rectus muscles did amblyopia develop." He did not say how he obtained this almost miraculous result—not even 1 case of amblyopia. He spoke of a paper in preparation. It is to be hoped that he will describe these aids to diagnosis and treatment which enable him to obtain such results.

Obviously, Dr. Smith has confused pseudoparetic hyperphoria with overaction of the inferior oblique muscle in paretic hyperphoria. The differential diagnosis is quite clear, as set forth by Bielschowsky.

Like many others, my colleagues and I have been doing myectomy of the overacting inferior oblique muscle, the results of which are not always satisfactory. We have been much interested in the operation of recession of this muscle at its point of origin. It is to be hoped that in his forthcoming paper Dr. Smith will discuss the results of this operation in his large number of cases, so that the value of this, as yet not well known, procedure may be determined. This operation is somewhat more formidable than myectomy of the inferior oblique muscle, but this offers no barrier to the experienced surgeon provided the results justify the procedure.

It is to be regretted that Dr. White did not share his rich experience in this field, and at least briefly discuss my paper. I never for a moment have felt that I had the power to convince him, but I did hope to stimulate his interest sufficiently to provoke discussion.

I wish to thank Dr. Smith for his free criticism in the discussion of my paper. It is by this means that one learns and is stimulated to further study and progress.

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EFFECT OF CHEMICAL WARFARE AGENTS ON THE HUMAN EYE

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With the possibility of gas warfare, it becomes apparent that clinical investigation of chemical agents so employed and their effects on the human eye is of paramount importance. Because of the paucity of literature on the subject, particularly in relation to the human eye, and the urgency for investigation of many aspects of the problem, it is deemed advisable to present these clinical observations as a basis for further studies. This paper was stimulated by the work of Scherling, Overholt and Stahmer [1] on the treatment of burns of the skin due to chemical agents and is part of a program of clinical investigation of chemical warfare agents at a station hospital.

The material for this study consisted of personnel at a chemical warfare arsenal.

Prior to the ophthalmologist's arrival at the station hospital, 87 persons with chemical burns of the eye had been inpatients. Of the total number of casualties thus observed, 2 were caused by liquid mustard gas (dichloroethylsulfide), 60 by mustard gas vapor, 17 by liquid lewisite (betachlorovinyldichloroarsine) and 8 by hexachloroethane. The total time lost in the hospital by these patients was four hundred and fifty-four days, with an average of five and two-tenths days per patient. For the casualties caused by liquid mustard gas the average loss of time was ten and five-tenths days; for those caused by mustard gas vapor, seven days; for those caused by lewisite vapor, four and seven-tenths days, and for those caused by hexachloroethane, three and seventy-five-hundredths days. Grossly visible corneal ulceration was encountered only with mustard gas, 2 casualties each being due to the liquid and the vapor. The diagnosis made grossly for all these patients was "chemical conjunctivitis," and all were discharged as "improved" or "well."

The following discussion will be limited to patients observed by the authors. Detailed examinations were conducted on all these patients, including repeated observations with the slit lamp and the corneal microscope. All were examined for corneal damage with and without a 2 per cent solution of sodium fluorescein.

Forty patients were examined and kept under observation. Seventeen of these patients were exposed to mustard gas vapor, and 1 was exposed to liquid mustard gas; the injuries of 5 patients were caused by lewisite vapor, and 2 others, although exposed to this agent, incurred burns of one eye from liquid lewisite; 5 patients received burns from hexachloroethane, 3 from white phosphorus fumes and 1 from white phosphorous spill; 2 patients were burned with arsenic trichloride and 3 with thermate.[1a] One patient's burn was purely a reaction to BAL solution.

Table 1 gives the over-all picture in these cases.

It should be mentioned that none of these patients actually needed hospital care, although several were admitted to permit more frequent study. None of the patients required more than twenty-four hours of absence from actual work. In the case of the burn due to the liquid mustard gas only this short period was necessary because but one eye was affected. Cycloplegia was instituted with 2 and 4 per cent solutions of homatropine hydrobromide to prevent long periods of disability. All the eyes but one returned to their previous status. This eye, burned by liquid mustard gas, is still under observation for cyclic degeneration of the cornea.

The following cases illustrate typical injuries due to the various agents, except for case 2, which was the only instance of a burn from liquid mustard gas in the series.

REPORT OF CASES

CASE 1.—A private first class, a healthy white man, in the Chemical Warfare Service was assigned to the toxic gas yard, where he was engaged in steam cleaning of cylinders which had contained liquid mustard gas. Since he did not use the gas mask provided him, he was constantly exposed to mustard gas vapor.[2] He was able to smell the gas constantly in the air but was well for three days. On the fourth day he experienced a

1. Scherling, S. S.; Overholt, B. M., and Stahmer, K. H.: Treatment of Burns Due to Chemical Warfare Agents, Bull. U. S. Army M. Dept., March 1944, no. 74, pp. 52-62.

2. Cowell, E. M.: Chemical Warfare and the Doctor, Brit. M. J. **2**:778-781 (Oct. 14) 1939.

sensation like that of a foreign body in both eyes. The next day the irritation had increased in intensity and was accompanied by photophobia, blepharospasm, redness and tearing. These symptoms increased in severity with each successive day. Nevertheless, he continued to perform his duties with efficiency. On the eleventh day he was referred to the station hospital by his commanding officer, who had noticed his difficulty. No treatment had been employed up to that time.

When first seen, he appeared to be in some distress. He avoided the light; his eyes were rather red, and lacrimation was evident on casual inspection.

Examination at this time revealed bilateral blepharospasm of severe degree. The eyelids could be kept apart only after instillation into the conjunctival sac of several drops of a 2 per cent solution of butacaine sulfate. There were slight edema and reddening of the lid margins. No vesicles were apparent. Vision, after topical analgesia, was 20/30 in each eye. The tarsal conjunctiva was slightly injected, and the bulbar portion manifested no edema, necrosis, hemorrhage or discharge. The vessels were moderately dilated, and those in the paralimbal region showed numerous saccular and fusiform aneurysmal dilatations. Throughout this membrane the vessels appeared to be increased in tortuosity and varied greatly in caliber. The vascular injection was most pronounced in the interpalpebral areas and faded toward the fornices. The cornea stained in punctate fashion, most profusely in the pupillary zone. The entire corneal epithelium appeared edematous and greasy. Although there was much dilatation of the limbal loops, vascularization of the cornea was not evident. The dichotomously branching nerve fibers in the cornea seemed to have increased remarkably in number and visibility. The iris presented no abnormalities, and the anterior chamber was optically empty. The tactile tension was within normal limits. There were no pathologic changes in the media or in the fundus of either eye.

The diagnosis was keratoconjunctivitis due to mustard gas vapor.

Cycloplegia was induced with 4 per cent homatropine hydrobromide, and the patient was admitted to the hospital. Here, instillation of homatropine was repeated daily for three days, and a solution of camphor water and epinephrine was used at frequent intervals.

On his second day in the hospital the photophobia and blepharospasm were mild, and the edema and erythema of the lids persisted to the same degree as before. There was no discharge. The tarsal conjunctiva was normal, and the bulbar conjunctiva showed moderate engorgement, with the same changes in the blood vessels as those previously noted. No hemorrhages were discernible. The cornea stained with fluorescein in punctate fashion, but to a lesser degree. The corneal edema appeared as before. No further changes had occurred.

On the fourth day in the hospital the camphor and epinephrine solution was replaced with glycerin. Cycloplegia was maintained in the same fashion. In twenty-four hours examination revealed the following changes: The injection of the bulbar conjunctiva had practically disappeared; the vascular changes in this membrane persisted; the corneal edema had completely cleared up, and the epithelium no longer stained with fluorescein. At this time the corneal nerves were as numerous and as easily visible as before.

The patient was discharged from the hospital. The use of homatropine was discontinued, and he was instructed to continue instillations of glycerin three times a day.

On the eighth day after he was first seen, examination of the cornea gave completely normal results, and vision was 20/20 in each eye. At this time the corneal

TABLE 1.—*Data on Ophthalmic Injuries Due to Chemical Warfare Observed in Forty Patients*

Case No	Agent *	Degree of Injury	Casualty	Duration of Signs	Treatment †
1	Hl	Severe	Yes	Current	Cycloplegia; curettage; C & E ‡; sulfathiazole
2	Hv	Severe	Yes (1 day)	7 days	Cycloplegia; glycerin (right eye); C & E (left eye)
3	Hv	Moderate	Yes (1 day)	7 days	Cycloplegia; glycerin (right eye); C & E (left eye)
4	Hv	Moderate	No	6 days	Cycloplegia; glycerin (right eye); C & E (left eye)
5	Hv	Slight	No	5 days	Cycloplegia; glycerin (right eye); C & E (left eye)
6	Hv	Slight	No	3 days	Cycloplegia; glycerin (right eye); C & E (left eye)
7	Hv	Very slight	No	3 days	Glycerin (right eye); C & E (left eye)
8	Hv	Very slight	No	1 day	Glycerin (right eye); C & E (left eye)
9	Hv	Very slight	No	24 hours	Cycloplegia; glycerin
10	Hv	Slight	No	5 days	Cycloplegia; C & E
11	Hv	Severe	Yes (2 days)	5 days	Cycloplegia; C & E
12	Hv	Severe	No	6 days	Cycloplegia; glycerin
13	Hv	Slight	No	5 days	C & E
14	Hv	Moderate	No	6 days	Cycloplegia; C & E
15	Hv	Moderate	No	8 days	P-E §
16	Hv	Severe	Yes (2 days)	8 days	Cycloplegia; C & E
17	Hv	Moderate	No	8 days	C & E
18	Hv	Severe	No	14 days	C & E
19	Ll	Moderate	No	24 hours	P-E
20	Ll	Moderate	No	2 days	P-E
21	Lv	Slight	No	1 day	P-E
22	Lv	Slight	No	1 day	Epinephrine hydrochloride (1:3,000)
23	Lv	Slight	No	1 day	Epinephrine hydrochloride (1:3,000)
24	Lv	Slight	No	1 day	Epinephrine hydrochloride (1:1,000)
25	HC	Slight	No	1 day	P-E
26	HC	Severe	Yes (2 days)	7 days	P-E
27	HC	Moderate	No	4 days	P-E
28	HC	Slight	No	2 days	P-E
29	HC	Slight	No	2 days	C & E
30	WP spill	Severe	No	1 day	3% copper sulfate; P-E
31	WPf	Moderate	No	1 day	3% copper sulfate; P-E
32	WPf	Moderate	No	1 day	3% copper sulfate; P-E
33	WPf	Severe	Yes (1 day)	4 days	C & E; P-E
34	WPf	Very slight	No	3 days	Boric acid; epinephrine
35	Ther	Slight	No	4 days	P-E
36	Ther	Slight	No	3 days	C & E
37	Ther	Severe	Yes (1 day)	10 days	Boric acid; P-E
38	AT	Severe	Yes (1 day)	14 days	Dilute BAL solution
39	AT	Moderate	No	3 days	Cycloplegia; sulfathiazole (3 per cent ointment)
40	BAL	Severe	No	1 day	P-E

* In this table, Hl indicates liquid mustard gas; Hv, mustard gas vapor; Ll, lewisite liquid; Lv, lewisite vapor; HC, hexachloroethane; WP, white phosphorus particles; WPf, white phosphorus fumes; Ther, thermate; AT, arsenic trichloride, and BAL, bal solution.

† In all cases except case 1, which was current at the time of writing, treatment resulted in restoration of the status quo ante.

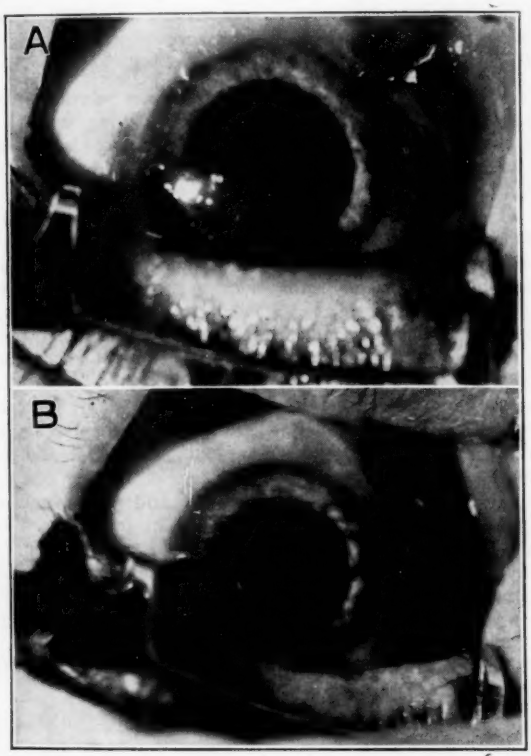
‡ C & E indicates a solution of 4 per cent camphor water and 8 per cent epinephrine hydrochloride (1:1,000) in distilled water.

§ Phenacaine-epinephrine ointment consists of phenacaine hydrochloride, 1 per cent; epinephrine hydrochloride, 2 per cent; water, 1 per cent; wool fat, 10 per cent, in a base of sterile white petrolatum, 86 per cent.

nerves were no longer visible, but the changes in the blood vessels of the bulbar conjunctiva remained.

The essential features in this case were: (1) the presence of corneal damage, which was transient and reversible; (2) the limitation of the injury to the exposed portions of the eyes [3]; (3) the suggested effects on the vessels of the bulbar conjunctiva; (4) the peculiar type of corneal edema, and (5) the increased visibility of the corneal nerves.

Case 2 (figure).—We first saw this patient approximately one month after he had been splashed with liquid mustard gas. He suffered first and second degree burns of the skin, which were of typical appearance, as described by Scherling, Overholt and Stahmer.[1] In addition, he received a splash of liquid mustard gas in his left eye. He had been given general treatment for his injuries in the hospital. In fifteen days he was discharged, and his eyes were treated with emollients because of the persistence of redness in his left eye.



A (December 14) photograph of an eye with burn due to liquid mustard gas, showing vesicle; *B* (December 31), photograph of the same eye as that shown in *A*, with flat, refractile facet. Photographs by Capt. Royal M. Williams.

When he was first seen by us, he complained of redness of the left eye, photophobia and the sensation of a foreign body. At that time vision (with correction) was 20/20 in the right eye and 20/40 in the left eye. The lids were normal in all respects, and there was moderate blepharospasm. There was no lacrimation or discharge, and only a minimal amount of injection of the tarsal conjunctiva was evident. The bulbar conjunctiva showed a slight amount of vascular congestion, which was generalized. There could be seen, with difficulty, several minute, fusiform aneurysmal dilatations of the vessels in the region of the limbus, to the temporal side and below. The vessels were moderately tortuous. No hemorrhages, edema or necrosis was discernible. A faint ciliary blush surrounded the limbus, and the limbal loops were congested but showed no evidence of invading the cornea. At 12 o'clock, about 3 mm. from the limbus, a bleb, 1 mm. in diameter and elevated about 1.5 mm., was noted. This was surrounded by a grayish zone of infiltration, 2 mm. in diameter. The bleb was highly refractile and did not stain with fluorescein. The endothelium was notably bedewed, and many corneal nerves were easily visible. A minimal zone of epithelial edema lay adjacent to the bleb. The anterior chamber was optically empty, and the iris showed no pathologic change. Intraocular tension was not increased.

Cycloplegia was induced with atropine, and a solution of camphor and epinephrine was prescribed for instillation. The patient volunteered the information that when the cycloplegia was effective the eye was almost free of discomfort.

Although the patient had been instructed to return much sooner, he did not do so until nineteen days later. At this time the aforedescribed symptoms and signs were unchanged; in addition, the bleb was now 1 mm. larger and had formed a crater which stained with fluorescein and seemed to extend below Bowman's membrane. The area of infiltration was much increased. A second bleb was beginning to form at 6 o'clock, 3 mm. from the limbus. This did not stain. The same treatment was continued except that an ointment containing 3 per cent sulfathiazole was also prescribed.

Twenty-six days after the first examination the superior ulcer had been converted into a flat, refractile, nonstaining facet. The epithelial surface of the entire cornea was irregular, and there was generalized subepithelial infiltration. This appeared to extend into the stroma. The inferior bleb now measured 1 by 1 by 1 mm. and did not stain. The limbal loops showed still greater congestion but did not extend beyond the limbus. The bedewing of the endothelium was still pronounced. There was no injection of the ciliary processes. The tarsal and bulbar conjunctivas appeared normal. The corneal nerves could not be seen because of the severe infiltration of the cornea.

At this time, with the use of anesthesia obtained by the instillation of 2 per cent butacaine hydrochloride, the corneal epithelium was curetted and the eye closed with a dry dressing.

Two days later the patient stated that he had no discomfort. Epithelial regeneration was complete. The bulbar and tarsal conjunctiva was moderately congested, and there was a slight amount of ciliary injection. The cornea did not stain with fluorescein, and the window reflex was regular. The entire subepithelial area was greatly infiltrated. The same treatment was continued.

Five days later the patient had no complaint. Vision was 20/30 in the left eye. There were slight blepharospasm and edema of the lid. The conjunctival injection had practically disappeared, and there was no ciliary injection. The entire cornea showed a greasy-appearing edema of the epithelium, and endothelial bedewing was pronounced. There were several minute areas of deep punctate staining in the cornea. Blebs, similar to those already described, had reappeared in several other areas of the cornea. Cycloplegia was maintained with atropine, and the same treatment was continued.

The patient did not return for three weeks. At this time the conjunctiva was entirely normal, and there was no ciliary injection. The limbal loops remained congested but did not infiltrate the cornea. The process previously described had apparently repeated itself, for

3. Gas Injuries to the Eyes, Lancet **2**:756-757 (Sept. 30) 1939.

there was now the refractile facet, surrounded by a zone of infiltration beneath the epithelium and extreme edema of the endothelium, which give a classic orange peel [4] appearance to the cornea. Corneal nerves were again numerous and conspicuous.

One week later the patient had no complaint except minimal photophobia at the end of a day's work. Vision was 20/40 in the left eye. The conjunctiva was normal in appearance except for the several minute, aneurysmal dilatations that persisted, and there was no vascularization of the cornea. The original facets seemed to have returned; they were nonstaining and slightly larger than before. The corneal epithelium seemed normal and did not stain with fluorescein. Subepithelial infiltration was slight and was most pronounced around the facets. The endothelium was less edematous. The anterior chamber was optically empty, and the iris appeared normal. At this time the instillation of atropine was discontinued because of the onset of catarrh due to its use. Use of the solution of camphor and epinephrine and of the sulfathiazole ointment was continued.

Eight days later the left eye presented approximately the same picture; in addition, both facets had again become blebs and did not stain.

During the entire course of the injury the intraocular tension remained normal, and no cells were seen in the aqueous. There were no abnormalities in the media or the fundus. The patient will continue to be examined at regular intervals, and treatment will vary according to the symptoms and signs and their severity.

Here, the chronicity of the corneal damage and the noninflammatory cyclic degeneration of the cornea are the outstanding features. It is apparent that, in contrast to the effect of the vapor, liquid mustard gas penetrates deeply. The absence of keratitic precipitates, free cells in the aqueous and inflammatory changes in the iris seems to indicate that the breakdown products of the cornea, although irritating to that membrane itself, do not stimulate the expected vascular response.

This case is still current, and subsequent progress of the abnormalities will be reported.

CASE 3.—An officer in the Chemical Warfare Service was present on the line when a leak of lewisite vapor occurred. Although he believed that he had not been exposed, he almost immediately instilled several drops of BAL solution into each eye. Within a few seconds he experienced burning and lacrimation and within an hour had moderate photophobia and blepharospasm.

Examination at this time revealed slight edema and erythema of the lids, moderate injection of the tarsal conjunctiva and severe congestion of the bulbar conjunctiva. The cornea did not stain, and its epithelium was not edematous. The anterior chamber and iris and the media and fundus were normal in both eyes.

An ointment containing phenacaine hydrochloride and epinephrine hydrochloride was prescribed, and relief was rapid. Twenty-four hours later his eyes had returned to normal.

This case demonstrates the irritant properties and the rapid and spontaneous recovery of the conjunctiva from the chemical insult of BAL solution itself.

CASE 4.—A civilian munitions worker while using thermate felt pain in both eyes. He was sent to the general dispensary, where the conjunctival sacs were irrigated with a solution of boric acid. On awakening the following day he had moderate photophobia and blepharospasm and lacrimation, but no discharge. His eyes appeared red and were painful.

Examination at this time revealed that vision was 20/30 in the right eye and 20/25 in the left eye. There was slight edema of the lids but no erythema. The tarsal conjunctiva was moderately injected, and there was patchy congestion of the bulbar conjunctiva. The corneal epithelium was impervious to fluorescein, and no edema was discernible. The anterior chamber and iris were normal and the media and fundus free of abnormalities in both eyes. In each inferior tarsal conjunctiva there were several whitish gray particles, each about the size of a grain of salt.

The granules were removed; the sacs were irrigated, and an ointment containing phenacaine and epinephrine was prescribed. The patient returned in five days. Examination at this time failed to elicit any signs of disease or injury.

This patient presented the picture of the usual chemical conjunctivitis caused by nonescharotic agents. The reaction was further emphasized by a conjunctival foreign body reaction. The absence of a discharge is to be noted.

CASE 5.—A male civilian munitions worker was present at a lewisite spill and felt something strike his right eye. Within four minutes this eye had been irrigated, and BAL solution had been instilled into both eyes.

The patient was first examined twenty-four hours later. At this time the left eye revealed no sign of disease or injury. There were moderate photophobia and blepharospasm of the right eye. Lacrimation was slight, and there was no discharge. The tarsal conjunctiva showed minimal injection, and the bulbar conjunctiva was moderately congested. No abnormalities of the conjunctival vessels could be noted. The corneal epithelium showed no edema and took no stain. Corneal nerves were not visible. The anterior chambers and irises were normal, and the media and fundi showed no pathologic changes.

An ointment containing butacaine and metaphen was prescribed, and the patient returned in four days. At this time he had no complaints, and examination of his right eye revealed no abnormalities except slight congestion of the limbal loops. The same treatment was continued. One week later there were no discernible pathologic changes in the right eye.

This case illustrates the excellent decontaminating effect of BAL solution.

CASE 6.—A civilian munitions worker who was employed with the previous patient was told that his eyes had suddenly turned red. He had experienced few, or no, symptoms of discomfort despite being aware of the lewisite odor. Within several minutes BAL solution had been dropped into the conjunctival sacs.

The patient was first examined the following morning. At this time he stated that he had experienced no change in visual acuity. He had slight photophobia and no blepharospasm. There was no lacrimation or discharge, and only slight vascular congestion of the bulbar conjunctiva in the interpalpebral area was noted. The corneal nerves were not seen; the epithelium was not edematous, nor did it stain with fluorescein. The anterior chamber, iris, media and fundus of both eyes were free of abnormalities.

An ointment containing phenacaine and epinephrine was prescribed.

The patient returned in two days. At this time he had no complaints, and examination failed to reveal any abnormalities.

This case, again, illustrates the efficacy of BAL solution.

4. Mann, I.: Mustard Gas Lesions of the Eyes, Brit. M. J. **1**:353-354 (March 14) 1942.

CASE 7.—A civilian munitions worker, while employed on the white phosphorus line, encountered a spill. He immediately jumped into the pool of water provided for that purpose and after several minutes was removed to the station hospital by ambulance.

Within twenty minutes after the accident examination revealed numerous areas on his clothing and the skin of his face and neck that were smoking. Smoke was also emanating from the conjunctival sacs.

Cursory examination of his eyes revealed several particles of white phosphorus embedded in the bulbar and tarsal conjunctivas. The sacs were immediately irrigated with a solution of boric acid. Several drops of a 2 per cent solution of butacine sulfate was instilled, followed one minute later by several drops of a 3 per cent solution of copper sulfate. After the irrigation with boric acid, the smoking of the conjunctivas ceased. The application of the copper sulfate was repeated several times within the next fifteen minutes. The embedded particles were removed. A few minutes after this slight blepharospasm developed, but this disappeared spontaneously within half an hour.

Examination about twelve hours later revealed vision of 20/20 in each eye. There was no lacrimation, and only an occasional small flake of mucus was noted in the lower fornices. The tarsal and bulbar conjunctivas were slightly injected except at the previously burned sites, where the congestion was moderate. The corneal epithelium showed no edema and did not stain. The rest of the examination revealed nothing abnormal. No further treatment was instituted.

Forty-eight hours later there was merely a suggestion of conjunctival injection, and the gray necrosis of the conjunctiva at the site of the white phosphorus particles had disappeared. No treatment was given or prescribed.

Two days later the eyes were reexamined and found free of any sign of disease or injury.

Several facts are illustrated in this case: (1) There is no contraindication to the use of copper sulfate in the eye; (2) copper sulfate is as efficacious in preventing the further combustion of white phosphorus in the conjunctiva as it is in the skin, and (3) the conjunctiva recovers rapidly from injury.

TABLE 2.—*Data on Ophthalmic Effects of Various Chemical Warfare Agents**

Case No.	Visual Loss	Photophobia	Blepharospasm	Edema and Erythema of Lids	Tarsal Conjunctival Injection	Bulbar Conjunctival Injection	Conjunctival Vessels ‡	Corneal Stain §	Corneal Edema ‖	Infiltration	Corneal Nerves Visible	Vascularization	Inflammation of the Iris	Ciliary Injection	Anterior Chamber (Cells)	Tactile Tension	Agent †
1	+	++	++	++	+	++	I	P	++ and +++ Endo		+	—	—	++	—	—	Hl
2	—	++	++	++	+++	+++	I&T	P	+++	—	++	—	—	—	—	—	Hv
3	—	++	++	++	++	+++	I&T	P	+++	—	++	—	—	—	—	—	Hv
4	—	++	+	+	+	++	I&T	P	++	—	++	—	—	—	—	—	Hv
5	—	+	+	—	+	++	I&T	P	++	—	+	—	—	—	—	—	Hv
6	—	+	+	—	+	+	T	P	+	—	+	—	—	—	—	—	Hv
7	—	—	—	—	+	+	T	P	+	—	—	—	—	—	—	—	Hv
8	—	—	—	—	+	+	T	P	+	—	+	—	—	—	—	—	Hv
9	—	+	+	—	+	+	T&A	P	++	—	++	—	—	—	—	—	Hv
10	—	++	++	+	+	++	T&A	P	++	—	+	—	—	—	—	—	Hv
11	—	+++	++	++	+	+++	T&A	P	+++	—	+	—	—	—	—	—	Hv
12	—	+++	++	++	+	+++	T&A	P	+++	—	—	—	—	—	—	—	Hv
13	—	+	+	—	+	++	T&A	P	++	—	+	—	—	—	—	—	Hv
14	—	++	++	+	++	++	T&A	P	+++	—	++	—	—	—	—	—	Hv
15	—	++	++	+	++	++	T	P	++	—	+	—	—	—	—	—	Hv
16	—	+++	+++	++	++	+++	T&A	P	+++	—	+	—	—	—	—	—	Hv
17	—	++	++	++	+	++	T&A	P	++	—	+	—	—	—	—	—	Hv
18	—	+++	+++	+++	++	+++	T&A	P	+++	—	++	—	—	—	—	—	Hv
19	—	++	+	—	+	+	—	—	+	—	+	—	—	—	—	—	Ll
20	—	++	+	—	+	+	—	—	+	—	—	—	—	—	—	—	Ll
21	—	+	—	—	+	+	—	—	—	—	+	—	—	—	—	—	Lv
22	—	+	—	—	+	+	—	—	—	—	—	—	—	—	—	—	Lv
23	—	+	+	—	—	+	—	—	—	—	—	—	—	—	—	—	Lv
24	—	—	—	—	—	+	—	—	—	—	+	—	—	—	—	—	Lv
25	—	—	+	—	+	+	—	—	—	—	—	—	—	—	—	—	HC
26	—	—	+	+	+	+	—	—	—	—	—	—	—	—	—	—	HC
27	—	—	—	+	—	+	—	—	—	—	—	—	—	—	—	—	HC
28	—	—	—	—	—	+	—	—	—	—	—	—	—	—	—	—	HC
29	—	—	—	—	—	+	—	—	—	—	—	—	—	—	—	—	HC
30	—	++	+++	+	+++	++	—	—	—	—	—	—	—	—	—	—	WP
31	—	+	+	—	+	+	—	—	—	—	—	—	—	—	—	—	WPf
32	—	+	+	—	++	+	—	—	—	—	—	—	—	—	—	—	WPf
33	—	++	+	+	++	++	—	—	—	—	—	—	—	—	—	—	WPf
34	—	+	—	—	+	—	—	—	—	—	—	—	—	—	—	—	WPf
35	—	+	+	—	—	++	—	—	—	—	—	—	—	—	—	—	Ther
36	—	++	++	—	—	++	—	—	—	—	—	—	—	—	—	—	Ther
37	—	++	++	+	+	++	—	—	—	—	—	—	—	—	—	—	Ther
38	—	++	++	—	+	++	—	—	—	—	—	—	—	—	—	—	AT
39	—	+	+	—	—	+	—	—	—	—	—	—	—	—	—	—	AT
40	—	++	++	—	+	++	—	—	—	—	—	—	—	—	—	—	BAL

* In this table, the minus sign indicates absence of the sign; +, a slight reaction; ++, a moderate reaction, and +++, a severe reaction.
† Hl indicates liquid mustard gas; Hv, mustard gas vapor; Ll, lewisite liquid; Lv, lewisite vapor; HC, hexachloroethane; WP, white phosphorus particles; WPf, white phosphorus fumes; Ther, thermate; AT, arsenic trichloride, and Bal, Bal solution.
‡ I and I&T indicate irregular caliber; T, tortuous vessels and A, aneurysmal dilatations.
§ P indicates punctate and linear stained patches.
‖ Epithelium only is referred to, except when endothelium is also indicated.

In table 2 pertinent data for injuries caused by the various types of chemical agents are compared.

COMMENT

The foregoing tables and case reports indicate a parallelism between the severity of the clinical symptoms and the signs and severity of the injury to the eyes. Photophobia and blepharo-

spasm are constant complaints, particularly when corneal damage is present. These symptoms are easily relieved by institution of cycloplegia. For this purpose homatropine is preferred to atropine. Since the corneal damage is transient and reversible, only additional loss of effectiveness would result from prolonged use of cycloplegia induced with atropine. Use of homatropine can be repeated daily to maintain its effect.

The bulbar conjunctiva appears to suffer more from insult than does the tarsal conjunctiva, probably since it is exposed. This observation is borne out by the concentration of vascular congestion in the interpalpebral areas.

Mustard gas vapor, if the concentration is sufficiently high, or liquid mustard gas may act directly on the exposed blood vessels, injuring them sufficiently so that irregularities in caliber and discrete dilatations are formed.[5] Whether these changes are reversible or not will require observation over a greater length of time.

The permeability of the corneal epithelium to fluorescein after exposure to mustard gas is a constant feature in cases of injury from the vapor of this agent. This observation is contrary to the reports of some authors.[6] The staining occurs quickly and in punctate fashion, indicating that the burn is a keratoconjunctivitis rather than a conjunctivitis only.[7] Mustard gas vapor produces rather characteristic edema of the corneal epithelium, the appearance being greasy and the process reversible. This phenomenon endures longer than does the permeability to stain.[8]

Since infiltration has not been observed after exposure to the vapor, it is inferred that damage does not extend beneath Bowman's membrane. In burns due to liquid mustard gas, however, Bowman's membrane is not a formidable barrier, and the injury can extend throughout the stroma and produce edema of the endothelium.

The absence of exudate and cells in the aqueous and of changes in the iris is provocative evidence that the products of corneal breakdown are not toxic if absorbed into the aqueous and that mustard gas does not pass unchanged through the cornea.[5]

Despite the fact that lewisite liquid and lewisite vapor have been proved to be as destructive to the skin as is mustard gas in corresponding form and dosage, the reported cases of contamination of the eyes show little serious effect. It should be borne in mind, however, that lewisite is productive of symptoms almost immediately and that mustard gas is not. Thus, first aid for lewisite burns can be instituted with little loss of time.[9]

A study of the present cases cannot but give the impression that when a substance other than the vesicants or the compounds intermediate in their manufacture is the toxic agent, the pathologic process is that of chemical conjunctivitis. These cases also present sufficient evidence to demonstrate the high resistance of the corneal epithelium to the nonvesicant compounds.

The increased visibility of the corneal nerve fibers in eyes which have been burned with mustard gas may be due to temporary changes in the refractive indexes of the various elements of this membrane.

In none of these cases was there any evidence of increased intraocular pressure. In the only case in which the corneal damage was possibly sufficient to cause secondary glaucoma a tension of about 20 mm. (Schiøtz) was repeatedly manifested. Because of the endothelial bedewing in this eye, the tension was measured accurately. In the rest of the cases the intraocular tension was measured by tactile means only.

To conclude, certain inferences may be safely drawn from even this relatively small number of cases.

If one eye only is affected by liquid mustard gas, the patient need not become a casualty and, indeed, need not become noneffective for more than a day or two. Exceptions occur when binocular vision is essential for efficiency.

Mustard gas vapor when it affects the eye only, unless present in extremely high and maintained concentrations (an unlikely circumstance), need not result in casualties.

Casualties from vesicant agents need exist as such for only two days to two weeks, and the casualty time and the duration of symptoms and signs correspond [10] with the clinical severity of the burn.

Mustrad gas vapor produces chemical keratitis, in addition to conjunctivitis, and it is the former

5. Gresser, E. B.: Ocular Injuries in Chemical Warfare, Hebrew M. J. **1**:183-188, 1943.

6. Hughes, W. F., Jr.: Mustard Gas Injuries to the Eyes, Arch. Ophth. **27**:582-601 (March) 1942. Gresser.[5] Mann.[4]

7. Aitken, R. S.: Effects of Accidental Exposure to Mustard Gas Vapor, Lancet **2**:602-603 (Nov. 13) 1943.

8. Matthews, J. L.: Ophthalmic Injuries of War, War Med. **4**:247-261 (Sept.) 1943. Mann.[4]

9. Cogan, D. G.: Lewisite Burns of the Eye, J. A. M. A. **122**:435-436 (June 12) 1943.

10. Warthin, A. S., and Weller, C. V.: The Pathology of the Skin Lesions Produced by Mustard Gas (Dichlorethylsulphide), J. Lab. & Clin. Med. **3**:447 (May) 1918.

which must be treated to reduce the casualty time, diminish discomfort and prevent infection. The conjunctival inflammation is self limited unless infection supervenes.

More study is necessary to determine whether or not the damage to the exposed blood vessels due to the vesicants is reversible.

Use of glycerin, because of its hygroscopic effect, or for other reasons, is recommended to combat the corneal edema that accompanies keratoconjunctivitis due to mustard gas vapor. The suggestion is made that such treatment be employed more frequently in the clinic and in the laboratory.

Liquid mustard gas produces a deep and persistent cyclic corneal degeneration, but probably does not reach the aqueous in unchanged form, as indicated by the lack of inflammatory signs in the anterior segment of the eye affected.[11]

Although lewisite acts as a powerful vesicant on epithelial tissue, the immediate appearance of symptoms permits a similarly early decontamination with BAL used as a solution or an ointment, a substance which has proved to have a high degree of efficacy.

Contamination of the conjunctiva with particles of white phosphorous should be treated as it is elsewhere on the body surface, the medication including the immediate use of a copper sulfate solution.[8]

Compounds such as thermate, hexachloroethane and white phosphorous vapor usually produce conjunctivitis of short duration.

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11. Gilchrist, H. L., and Matz, P. B.: The Residual Effects of Warfare Gases: Chlorine and Mustard, United States War Department, Chemical Warfare Service, 1933.

RELATION OF BLOOD DYSCRASIA TO RETINOPATHY

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NEW YORK

According to the present concept, retinopathy implies manifestations in the fundus of hypertension; renal disease; diabetes; retinal edema and exudates secondary to various forms of optic neuritis and papilledema; localized disease of blood vessels, such as Coats's disease (retinitis exudative) and von Hippel's disease (angiomatosis of the retina); senile degenerative disease of Bruch's membrane and choriocapillaris, and, finally, diseases of the blood.

Actually, all types of retinopathy are based on localized structural changes in the blood vessels and capillaries, irrespective of the cause. With the exception of tuberculosis of the vessels and angiomatosis, these changes in the blood vessels are produced by some type of blood dyscrasia, primary or secondary.

Since nutrition of the walls of small vessels and capillaries depends on the quality as well as the quantity of the blood within, qualitative or quantitative reduction results in degenerative changes. In cases of early hypertension with localized quantitative reduction, retinopathy is limited to the arteries. Later in the disease, when the renal function is affected, change in the chemical constituents of the blood, or secondary blood dyscrasia, with its effect on the nutrition of capillaries and venules, is responsible for the appearance of hemorrhages and exudates. In cases of acute nephritis secondary anemia must play an important role in effecting structural vascular changes, which are the basis of severe hemorrhagic manifestations. In other words, blood dyscrasias have to be reckoned with even in the retinopathy of renal disease. This explains the similarity of the fundus picture associated with diseases of the blood to that present with nephritis.

APPEARANCE OF THE FUNDUS IN VARIOUS BLOOD DYSCRASIAS

The following blood dyscrasias may be responsible for ophthalmic manifestations: (1) chlorosis, (2) pernicious anemia and sprue, (3) von Jaksch anemia (anemia infantum pesudoleukemia), (4) secondary anemia, (5) sickle cell anemia, (6) aplastic anemia, (7) hyperplastic anemia, (8) erythremia (polycythemia vera), (9) secondary polycythemia, (10) purpura hemorrhagica, (11) hemophilia, (12) scurvy, (13) lipemia, (14) leukemia, (15) sepsis and (16) diabetes.

Chlorosis.—This condition is a hypochromic anemia of young adults, especially women; it is now rarely encountered. While the number of red blood cells is reduced, the reduction of hemoglobin is proportionately greater. The fundus is generally normal, though the blood vessels and the retina in general are pale. The presence of papilledema and a macular star with hemorrhages has been reported (Moore [1]).

Pernicious Anemia.—The origin of this disease is unknown. The red blood cell count is usually below 1,000,000, with a relatively high color index (hyperchromia). There is leukopenia, with lymphocytes predominating. The glands are not involved, and there is not much loss of fat. Free hydrochloric acid and lactic acid are absent in the stomach. Gastric symptoms are not prominent. The skin is lemon colored. There is an excess of urobilin in the stool. The disease is frequently associated with degeneration of the spinal cord. Reflexes are exaggerated at first and absent later.

Fundi: The fundi are normal in cases of the mild form of the disease. In cases of moderate severity, there is general pallor, and the blood vessels are small. Later, secondary hyalinization of the arterial walls creates a copper wire appearance. The low blood pressure is responsible for segmental fading simulating spasm, so that at first glance one has the impression of signs of essential hypertension, including arteriovenous crossing. In addition, the low diastolic blood pressure, together with a relatively normal intraocular pressure, may result in manifest pulsation of arteries, similar to that seen in cases of glaucoma or of aortic insufficiency. Necrosis of capillaries may result in the appearance of small hemorrhages. Thrombosis in veins may give rise to large hemorrhages. Spindle-shaped hemorrhages with central small white spots (leukocytic

Read at a meeting of the New York Society for Clinical Ophthalmology, April 3, 1944.

1. Moore, R. F.: Medical Ophthalmology, ed. 2, London, J. & A. Churchill, 1925.

clumping) have been observed (Collier,[2] Taylor[3]). In my own clinical experience retinal hemorrhages in cases of more advanced pernicious anemia have been rather common. Secondary optic nerve atrophy with loss of vision may occur, even in the absence of hemorrhages. With improvement of the patient, vision returns to normal, providing the hemorrhages have not been too extensive.

Sprue, with its effect on the gastric mucosa, produces a blood picture similar to that of pernicious anemia. Hydrochloric acid is present in the stomach. The sugar tolerance is low. Liver therapy has no effect.

Von Jaksch's Anemia.—This disease is one of early infancy. It seems to be a combination of severe anemia and leukemia, with enlarged spleen. The blood picture is similar to that of pernicious anemia, with leukocytosis, the mononuclear cells predominating. I have not found any report of the retinal features but have seen 1 case in which hemorrhages were present. There is no reason that such hemorrhages should not be observed if looked for.

Secondary Anemia.—This condition is frequently due to obscure gastric carcinoma. It occurs late in life. The blood picture is similar to that of pernicious anemia, but there is leukocytosis, of polymorphonuclear cell type. Progressive emaciation is present. Gastric symptoms are prominent. The supraclavicular glands may be palpable. Increased resistance is encountered over the gastric area. There is absence of hydrochloric acid in the stomach, but lactic acid is present. The skin is pale and of a saffron tint. Retinal hemorrhages may be present; the arteries are small and the retinal veins large. Soft, woolly patches may be seen.

Sickle Cell Anemia.—This anemia is secondary, of unknown origin; it is familial and occurs chiefly in the Negro race. The active stage is characterized by extreme weakness, dyspnea, abdominal pain, nausea and vomiting and pains in the muscles and joints. The liver is large, but the spleen is small; the lymph glands are enlarged. There is a greenish yellow discoloration of the sclera. Retinal hemorrhages occur. In the latent stage of the disease constitutional symptoms are not prominent. The blood picture is characterized by a decrease in the red cell count and in the hemoglobin concentration and by the presence of poikilocytes, polychromasia, anisocytes and characteristic crescent red blood cells (sickle cells). The reticulocytes are increased in number. Leukocytosis, with a count of 15,000 to 20,000 cells, is usually present.

Aplastic Anemia.—This disease is rapidly progressive; the origin is unknown. The acute form is fatal. The blood picture is based on a pathologic process in the bone marrow, which is yellow and fatty. This condition results in failure of red cell formation. The skin is yellowish, and there is a tendency to hemorrhage into the skin and mucous membranes. Hemorrhages into the retina occur (Carslaw and Dunn[4]). Paroxysmal fever is present. Polymorphonuclear cells are greatly reduced. The chronic form may develop in association with a severe infection, as well as late in the course of pernicious anemia.

Hyperplastic Anemia (hemolytic).—The occurrence of hemolysis represents an attempt to keep down the number of red cells. Embryonic (immature) red cells, normoblasts, macrocytes, microcytes, spherocytes and poikilocytes are present. The blood picture is similar to that of pernicious and of secondary anemia and often follows persistent hemorrhage, such as occurs with severe, recurrent epistaxis, gastric ulcer or hemorrhoids. Other common causes are favus and poisoning due to the sulfonamide compounds, dinitrophenol, arsphenamine and phenylhydrazine. Hemoglobinuria is frequently noted. Retinal hemorrhages are not uncommon.

Erythremia (polycythaemia vera; Vaquez-Osler disease).—In this disease there is hyperplasia of erythroblastic elements of the bone marrow. The condition must be distinguished from secondary polycythemia associated with congenital anomalies of the heart, pulmonary stenosis and emphysema and that occurring possibly at high altitudes. In the secondary form cyanosis is prominent, and the spleen is not enlarged. In the fundus only cyanosis and engorged retinal veins are seen. In polycythemia vera, however, the ophthalmic changes may include photophobia, scotoma (Friedenwald[5]) and hemianopsia. Ophthalmoscopic findings are large arteries, engorged cyanotic veins and, sometimes, papilledema and pronounced hemorrhages.

Treatment consists of venesection and irradiation or the use of irradiated phosphorus.

2. Collier, in Allbutt, T. C., and Rolleston, H. D.: System of Medicine, London, Macmillan & Co., 1910, vol. 7, p. 799.

3. Taylor, J.: Tr. Ophth. Soc. U. Kingdom **23**:1, 1913.

4. Carslaw, J., and Dunn, J. S.: Glasgow M. J. **73**:331, 1910.

5. Friedenwald, in Contributions to Medical and Biological Research Dedicated to Sir William Osler, New York, Paul B. Hoeber, 1919, vol. 1, p. 495.

Purpura Haemorrhagica. — A tendency to hemorrhages into the skin and mucous membranes is characteristic. The fundus is usually normal, but severe hemorrhages around the disk, as well as subretinal and infiltrating hemorrhages with edema, have been encountered.

Hemophilia.—This condition is associated with deficiency of prothrombin. The fundi are normal. Several years ago I saw a case in which intraocular hemorrhage resulted from slight trauma. Such hemorrhages were reported by Hirschberg, in 1879,[6] and Bramwell, in 1886.[7]

Scurvy.—A vitamin C deficiency is responsible. Retinal hemorrhages are not observed. Sometimes night blindness is caused by metabolic disturbance of the visual purple.

Leukemia.—The leukemia is chiefly of the lymphatic or the myelogenous type. Sometimes exophthalmos with chemosis is present. The fundus most commonly shows engorgement of retinal veins and extensive retinal hemorrhages. Sometimes it is yellowish pale. Small white patches surrounded by a red zone (red cells surrounding clumps of white cells) may be observed.

Lipemia.—Fat is present in the blood in emulsified state. Lipemia is encountered most commongly with diabetes, alcoholism, starvation, asphyxia, phosphorus poisoning (White[8]), trench nephritis (Moore[9]) and xanthomatosis (Wile, Eckstein and Curtis[10]). The manifest sign (white retinal blood vessels) is seen only in cases of diabetes with acidosis. Wagener[11] reported this sign in cases of leukemia in which irradiation treatment has been given.

Three forms of lipids are found in the blood: triglycerite of higher fatty acids, phosphatids and cholesterol. The greatest increase is in fatty acids; then, in cholesterol and least, in phospholipids. To be seen, the lipid must be emulsified (Wishart[12]). The highest value (48 per cent) was recorded by Chase, in 1927.[13]

Sepsis.—The ophthalmologist is frequently called on to make examination in a case of septic endocarditis with a positive or a doubtful blood culture. Only in cases of real sepsis are the ophthalmoscopic findings positive. Retinal hemorrhages, Roth's spots (spindle-shaped hemorrhages with a white center) and even papilledema are frequently seen. The presence of these changes is equivalent to the presence of the causative organism in blood culture. Embolism of the retinal artery, with the resulting ischemia and the cherry red spot in the macula, is not uncommon, even in cases of rheumatic endocarditis.

Diabetes.—Changes in the fundus, which many observers believe are secondary to associated arteriosclerosis, are similar to the alterations in cases of blood dyscrasia with secondary degeneration of the capillaries and veins. While arteriosclerosis and hypertension intensify the fundus picture, hemorrhages and retinal exudates are seen in patients with negligible arteriolar sclerosis, and even in children (Agatston[14]). Furthermore, this hemorrhagic tendency persists in persons the level of whose blood sugar is easily controlled by diet or insulin or both. It would seem as though some substance, or the lack of some substance, interfered with the nutrition of the capillaries or the veins, which in the retina are particularly delicate and vulnerable.

CONCLUSION

It is evident that absence of essential blood elements and changes in the chemical constituents of the blood are responsible for homeostatic nutritional disturbance, first, in the capillaries and, later, in the venules. This nutritional defect results in the escape of the blood contents, with production of various phases of retinopathy.

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6. Hirschberg: Arch. f. Augenh. **8**:174, 1879.
7. Bramwell, B.: Edinburgh M. J. **32**:101, 1886-1887.
8. White, H.: Lancet **2**:1007, 1903.
9. Moore, R. F.: Lancet **2**:1348, 1915.
10. Wile, U. J.; Eckstein, H. C., and Curtis, A. C.: Lipid Studies in Xanthoma, Arch. Dermat. & Syph. **19**:35 (Jan.) 1929.
11. Wagener, H. P.: Am. J. Ophth. **5**:521, 1922.
12. Wishart, M. B.: J. Metabolic Research **2**:199, 1922.
13. Chase, L. A.: Canad. M. A. J. **17**:197, 1927; Diabetic Lipemia Retinalis, J. A. M. A. **97**:171 (July 18) 1931.
14. Agatston, S. A.: Clinicopathologic Study of Diabetic Retinitis, Arch. Ophth. **24**:252 (Aug.) 1940.

TOXICOLOGY OF DICHLOROETHANE

I. EFFECT ON THE CORNEA

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For the past year and a half studies have been carried out in this laboratory on the toxicity of 1,2-dichloroethane (CH_2Cl-CH_2Cl). It was found that guinea pigs, mice, rats and rabbits were killed by only a few exposures of seven hours each to the vapor in concentrations as low as 400 parts per million. Dogs remained in good condition after nearly 200 exposures to a concentration of 400 parts per million, but with a concentration of 1,000 parts per million some of the animals died. The investigation is still in progress. This paper is concerned with one phase of the toxicity of dichloroethane, namely, its peculiar action on the cornea of certain species of animals.

A number of authors have observed that the eyes of dogs became cloudy after inhalation narcosis with dichloroethane.[1] This report presents observations on the corneal reaction to single and to repeated exposures to various concentrations of dichloroethane. It was shown that the effect could be produced without actual narcotization of the animals. It was also shown that clouding of the cornea could be reversed many times in the same animals, but that eventually the dogs became resistant to the effects of this chemical. The critical concentrations of dichloroethane which were required to produce the turbidity were determined. Of eleven species of animals studied, the turbidity was produced only in the fox in and in the dog.

EXPERIMENTAL PROCEDURE

The exposure chamber and the general method of procedure were the same as those employed in a previous study.[2] A large chamber was used in which many animals of different species could be exposed simultaneously. Four hundred liters of air was drawn through per minute, a flow which resulted in a complete change of air every seven minutes. Dichloroethane was volatilized at a constant rate, and the vapors joined the main air stream entering the chamber. It was possible to calculate the concentration in the chamber, and the figures so obtained were checked by daily chemical analysis of gas samples.

Four concentrations were employed: 3,000; 1,500; 1,000, and 400 parts per million parts of air. Each period of exposure was seven hours.

The eyes were removed immediately after death, fixed in a 3.8 per cent solution of formaldehyde, embedded in pyroxylin of low viscosity and sectioned. Sections were stained with Van Gieson's connective tissue stain and with hematoxylin and eosin.

RESULTS

I. Concentration of 3,000 Parts per Million.—A single seven hour exposure to a concentration of 3,000 parts per million was administered to 16 rabbits, 14 guinea pigs, 19 mice, 20 rats, 2 domestic hogs, 2 raccoons, 2 cats and 1 red fox. The fox and the raccoons had been exposed

From the Industrial Hygiene Research Laboratory, National Institute of Health, United States Public Health Service.

1. (*a*) Dubois, R., and Roux, L.: The Anesthetic Action and Toxicity of Ethylene Dichloride, Compt. rend. Acad. d. sc. **104**:1869, 1887. (*b*) Panas, N.: The Effect of Ethylene Dichloride on the Eye, ibid. **107**: 921, 1888. (*c*) Faravelli, E.: A Note on the Effect of Inhalation of Ethylene Bichloride on the Cornea, Arch. per le sc. med. **16**:70, 1892. (*d*) Steindorff, K.: The Effect of Some Chlorine Derivatives of Methane, Ethane and Ethylene on the Cornea of the Animal Eye, Arch. f. Ophth. **109**:252, 1922. (*e*) Kistler, G. H., and Luckhardt, A. B.: Pharmacology of Some Ethylene-Halogen Compounds, Anesth. & Analg. **8**:65, 1929.

2. Heppel, L. A.; Neal, P. A.; Perrin, T. L.; Orr, M. L., and Porterfield, V. T.: Toxicology of Dichloromethane (Methylene Chloride): I. Studies of Effects of Daily Inhalation, J. Indust. Hyg. & Toxicol. **26**:8, 1944.

seven hours previously to the vapor in concentrations of 1,000 and 1,500 parts per million, without their eyes being affected.

Only the red fox showed changes in the cornea. When the animal was removed from the chamber, a barely detectable turbidity was noted, which became readily apparent within six hours. Two days later the eyes were rather opaque. The animal refused food, appeared listless and died six days after the exposure. Histologic study revealed bilateral corneal edema, and the cornea of one eye showed scattered polymorphonuclear leukocytes in the substantia propria.

Fig. 1.—Typical corneal turbidity in a fox.

II. Concentration of 1,500 Parts per Million.—No corneal changes were observed in guinea pigs, rats or rabbits which were repeatedly exposed to dichloroethane in a concentration of 1,500 parts per million. Most of the animals died after the completion of 4 exposures.

Six dogs received a single exposure, lasting seven hours. In 1 of them the corneas showed no change; in another faint turbidity developed, while in the remaining 4 dogs there was intense clouding of both corneas. In the case of 1 dog the opacity cleared up within a week and returned when the exposure was repeated. Three dogs were exposed repeatedly to the vapor in a concentration of 1,500 parts per million. In all the animals there developed bilateral corneal opacity, which became intense forty-eight hours after the first exposure. One animal died after 5 exposures and another after 6 exposures. The third animal was killed after 30 exposures. The turbidity remained at maximal intensity.

Histologic examination was made of the eyes of 7 dogs. The eyes which were turbid at the time of death showed the following changes: (1) corneal edema, with swelling, separation and distortion of the fibers of the substantia propria; (2) degeneration and sloughing of the corneal endothelium, and (3) infiltration of polymorphonuclear leukocytes into the substantia propria, especially at the corneoscleral junction, and occasionally into the anterior chamber and the filtration angle. The eyes which had cleared before death were histologically normal.

III. Concentration of 1,000 Parts per Million.—A group of dogs received both single and repeated exposures to dichloroethane in a concentration of 1,000 parts per million. The detailed results are given in the protocols at the end of the report. The data may be summarized as follows:

1. A single exposure of seven hours to 1,000 parts per million led to symmetric turbidity of the corneas in 8 of 10 dogs. The process tended to clear from the periphery inward. It sometimes took as long as three weeks for partial regression.

2. Repeated exposures to dichloroethane were generally administered in series of 5, separated by a rest period of two days. The turbidity became increasingly intense during the 5 exposure days and tended to clear during the rest periods. In successive weeks the series of 5 exposures had less and less effect on the cornea. Finally, the cornea became almost completely resistant to the chemical. If exposures were resumed after an interval of rest of two to four weeks, the cornea still showed this resistant state.

3. The development of the corneal turbidity was always symmetric on the two sides, but the clearing process was sometimes limited to one cornea or to portions of a cornea. Cats, monkeys, chickens and various rodents exposed to dichloroethane in a concentration of 1,000 parts per million showed no changes in the eyes.

IV. Concentration of 400 Parts per Million.—Six dogs received repeated seven hour exposures to dichloroethane in a concentration of 400 parts per million. They were nearly always exposed on 5 days out of the week, and a two day period of rest intervened between the series of exposures. In the course of the first week a mild clouding was noted, which cleared entirely during the rest period. During the fifth week 5 exposures produced only a faint opacity of the corneas. By the tenth week the dogs failed to show even traces of turbidity at any time.

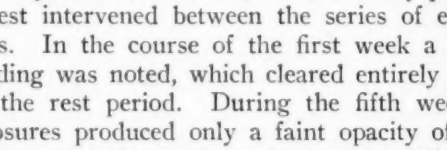

Fig. 2 (dog 1).—Typical clouding of the cornea after exposure to dichloroethane in a concentration of 1,000 parts per million. The opacity remained unchanged for many weeks.

COMMENT

The data reported here confirm the observations in other reports in showing that inhalation of dichloroethane was followed nearly always by the development of turbidity in both corneas of dogs. The entire cornea became opaque, and the process was associated with a great increase in its anterior curvature. Other authors have reported that the process did not occur in rabbits.[1e] We studied eleven species of animals and

obtained the corneal clouding only in dogs and in a red fox. The pathologic observations reported here agree with data in the literature except that not all investigators have noted an infiltration of polymorphonuclear leukocytes into the cornea.

In all published reports the dogs were stated to have been anesthetized with dichloroethane. Under these conditions clearing up of the turbidity was unusual and required several days or weeks. Only Steindorff [2d] described a case of unilateral clearing. When the animal was anesthetized a second time, the turbidity promptly returned and then did not disappear. In the present study it was found that anesthesia was not necessary to produce this phenomenon. Furthermore, in some animals the turbidity was reversed in less than two days, and clearing took place many times in the same eye. Several instances were noted in which only one eye cleared, and others in which merely a portion of the cornea lost its cloudiness.

In the present investigation it was noted that the dogs eventually became tolerant to dichloroethane and that the corneas no longer became cloudy after exposure. This is an interesting example of the development of a resistant state in a local tissue.

The basis of the lesion is believed to be injury to the posterior, or endothelial, surface of the cornea. According to the theory of Cogan and Kinsey,[3] the cornea is maintained in a state of relative deturgescence because of the resultant action of two forces. The corneal stroma has considerable imbibitory power and takes up fluid from the limbal vascular plexus. On the other hand, the cornea is continually in a deturgescent state because of osmotic forces acting on its surface. These forces depend on the fact that the epithelium and the endothelium of the cornea are semipermeable with respect to sodium chloride. Elimination of the osmotic forces by injury of the semipermeable membrane results in swelling and opacity of the cornea. For the cornea to remain transparent it must be maintained in a deturgescent state.

In some of our dogs which were exposed to a concentration of 1,000 parts per million, the turbid eyes did not show evidence of endothelial injury. In these animals, presumably, the semipermeability properties of the endothelial layers were disturbed, even though no histologic changes were manifest.

Apparently, the injury to the corneal endothelium is not caused directly by dichloroethane. When the material was injected into the anterior chamber,[1d] only severe iridocyclitis resulted. We carried out a few experiments in which the excised eyes of dogs were soaked in saline solution containing dichloroethane and others in which dichloroethane was injected into the anterior chamber. At the end of twenty hours there was no reliable difference between the behavior of the experimental eyes and that of the control eyes soaked in the saline solution.

No cases of injury to the human cornea from dichloroethane have been reported. That such injury might occur is possible, although improbable.

3. Cogan, D. G., and Kinsey, V. E.: The Cornea: V. Physiologic Aspects, Arch. Ophth. **28**:661 (Oct.) 1942.

SUMMARY

1. Exposure of dogs for seven hours to inhalation of dichloroethane in concentrations of 400, 1,000 and 1,500 parts per million led to bilateral swelling and turbidity of the corneas.

2. Development of the turbidity was always bilateral, but the clearing process sometimes involved only one eye.

3. When dogs were given repeated daily exposures to dichloroethane in a concentration of 1,000 parts per million, in series of 5 exposures, separated by rest periods of two days, they gradually became tolerant to the vapor. Eventually, no cloudiness developed after the exposures.

4. Of eleven species of animals tested for sensitivity of the cornea to dichloroethane, namely, the rat, mouse, rabbit, guinea pig, hog, cat, raccoon, fox, dog, chicken and rhesus monkey, only the fox and the dog showed cloudy corneas.

PROTOCOLS

Protocols are given for individual dogs exposed to dichloroethane in a concentration of 1,000 parts per million. The animals were exposed seven hours daily, usually 5 days a week, with a rest period of two days between the series of exposures.

Dog 1: *First Week.*—The corneas of both eyes showed slight turbidity six hours after the first exposure and intense clouding within forty-eight hours.

Next Eleven Weeks.—No change in the clouding was apparent. Both corneas remained intensely opaque.

Last Two Weeks.—The cornea of the right eye cleared partially from the periphery inward. The cornea of the left eye was unchanged.

Dog 2: *First Week.*—The corneas of both eyes were slightly turbid six hours after the first exposure, the turbidity reaching its maximum intensity in forty-eight hours. During a rest period of two days the cornea of the left eye remained very turbid, while the cornea of the right eye cleared entirely.

Second Week.—The right cornea was clear during the first 3 exposures; then it became turbid again. The left cornea remained intensely opaque. Over the week end (two days) the right cornea became clear again.

Third Week.—The right cornea was only slightly cloudy after 3 exposures. The left cornea remained opaque.

Fourth and Fifth Weeks.—The dog was ill, and no exposure was made.

Sixth to Fourteenth Week.—The cycle of clouding in the course of 5 exposures and the clearing over a rest period of two days was repeated over and over in the cornea of the right eye, for a total of eleven times. On successive weeks clouding developed more slowly and was less intense. During the last week only a faint haze was noted. The cornea of the left eye remained opaque during all this time.

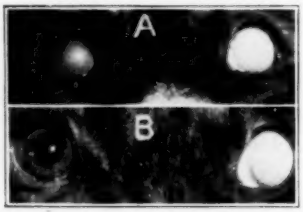

Fig. 3 (dog 2).—*A*, condition of the eyes immediately after a series of 5 exposures to dichloroethane in a concentration of 1,000 parts per million. *B*, photograph taken two days after the series of 5 exposures. The right eye has cleared, while the left eye remains cloudy.

Dog 3: *First Week.*—Bilateral corneal turbidity developed six hours after the first exposure and was intense within forty-eight hours.

Second and Third Weeks.—The dog was ill, and no exposure was made. The periphery of both corneas gradually cleared.

Fourth Week.—Exposures were resumed. Both corneas became completely clouded again.

Fifth to Ninth Week.—The animal was seriously ill, and no exposure was made. During this interval both corneas cleared until only a small central portion remained opaque.

Tenth Week.—Exposures were resumed. Both corneas became completely turbid again. During a two day rest period the peripheral portions cleared, while the central area remained turbid.

Eleventh Week.—The procedure and the results were similar to those in the tenth week.

Twelfth Week.—The corneas became completely turbid again. The animal died after 3 exposures.

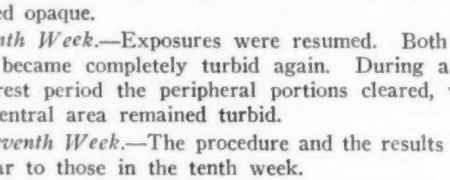

Fig. 4 (dog 3).—Corneas after exposure to dichloroethane (1,000 parts per million). The peripheral areas show clearing, while the central portions of the corneas remain cloudy.

Dog 4: *First Week.*—Bilateral corneal turbidity developed six hours after the first exposure and became intense within forty-eight hours. Over the week end turbidity cleared entirely except for a tiny spot on one eye.

Second Week.—Only slight turbidity was noted in either eye after 4 exposures. It cleared completely over the week end.

Third Week.—Faint turbidity was noted after 5 exposures. It cleared over the week end.

Fourth Week.—No turbidity developed. The animal became seriously ill.

Fifth to Ninth Week.—No exposures were given.

Tenth Week.—Both corneas became turbid after 4 exposures, but the process took longer to develop than during the first week. The process cleared completely over the week end.

Eleventh Week.—Mild turbidity developed in both corneas and cleared over the week end.

Twelfth Week.—Barely perceptible turbidity developed in both corneas after 4 exposures. The animal became sick and died.

Dog 5.—The animal received a single seven hour exposure. Bilateral corneal turbidity developed within six hours and became intense in forty-eight hours. The animal was observed for four weeks. No change was noted except slight clearing of the periphery of the right cornea. Daily exposures were then begun.

First Week.—The corneas of both eyes were entirely turbid on the second day. During a two day rest period the right eye showed clearing.

Second Week.—Turbidity returned to the periphery of the right cornea on the third day.

Third to Fifth Week.—During each week less turbidity developed in the cornea of the right eye than during the previous week, and during each week end the eye cleared almost entirely. The cornea of the left eye remained turbid.

Sixth Week.—The right cornea showed only a faint haze. The left cornea was opaque.

Dog 6.—The animal received a single seven hour exposure. Bilateral corneal turbidity was present six hours later and became intense within forty-eight hours. Gradual clearing of the periphery of the cornea took place over a period of four weeks. Then daily exposures were begun.

First Week.—Turbidity increased so as again to involve both corneas completely, after 3 exposures. Over the week end there was clearing of the periphery.

Second to Sixth Week.—The cycle was repeated each week. The process of clearing advanced further in the right eye. During the final week of exposure the cornea of the right eye remained almost entirely clear except for its central portion.

Dog 7.—The animal received a single seven hour exposure. Bilateral corneal turbidity developed. In nine days the left cornea became entirely clear, while the central part of the right cornea remained cloudy. After a second exposure of seven hours both corneas again became entirely clouded. In three days both eyes became clear except for a small portion of the right cornea.

Dog 8.—The animal received a single seven hour exposure. Bilateral corneal turbidity developed and cleared in a few days. After a second exposure of seven hours the turbidity returned. Within a few days it again cleared.

Dogs 9 and 10.—The animals received a single seven hour exposure to dichloroethane in a concentration of 1,000 parts per million. No corneal turbidity developed. Later they received a single seven hour exposure to a concentration of 1,500 per million. Both dogs then showed cloudy corneas.

JOHANNES MÜLLER

A SKETCH OF HIS LIFE AND OPHTHALMOLOGIC WORKS

BURTON CHANCE, M.D.

PHILADELPHIA

There is nothing so interesting and instructive as the lives and records of great men. For many years thoughts about Johannes Müller have engaged me, and for a long time I have wished to compile a chapter which, in addition to giving a brief description of the man and his personality, would revive in others memories of the part he took in the foundation of modern ophthalmology through his investigations of the physiology of the organ of vision.

Der Schuhmachermeister Matthias Müller. Frau Theresia Müller.

Fig. 1.—Portraits of Müller's parents.

Müller was born at Coblentz on the Rhine, July 14, 1801. He came of good common stock; his grandfather was a vine dresser, and his father, Matthias, was a shoemaker and saddler, in comfortable circumstances. Johannes was the eldest of five children, but he was the only one of whom one hears anything of importance. At school he excelled in mathematics and drawing and was a fine classical scholar. He translated the works of Plato and Aristotle and wrote Latin better, so his masters declared, than his native German.

His parents did what they could to give the intelligent boy all possible education. His father, however, determined that in time he should be apprenticed to a saddler, while his mother declared that his talents should be developed along naturalistic lines. Yet, as the family were seriously and devoutly religious, they wished that this eldest son might be dedicated to the church; so, when Johannes was 8 years of age, he delighted them by declaring that he wished to become a priest.

He collected plants and butterflies; yet all living objects in field and wood engaged his interest. Even in his boyhood Müller was decidedly independent in all that he studied and loved any work for its own sake.

He entered army duty in 1819, according to regulations, and served in the Engineer Corps. At the expiration of the term he decided to study medicine and immediately went up to the University of Bonn. This decision greatly dis-

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appointed his family, yet because of his persistence his high-minded mother became reconciled and lived to share his greatness. It was only after severe struggles that the love of science gained the mastery, and he said to a friend, "There I know what I have and whom I serve." He aspired to be a teacher. In the second year of his studies he became a candidate for a prize, the first to be offered by the University. This he won for an essay "On the Respiration of the Foetus." In December 1822 he received his degree, being then only 21 years of age.

The next three years were spent at the University of Berlin, where he came under the influence of Rudolphi, professor of anatomy and physiology, who soon became impressed by the exactness of the young man's powers of observation.

Müller, early realizing that he was not suited for medical practice, resolved to devote himself to the natural sciences. In 1826 he was appointed assistant in human and comparative anatomy in the University of Bonn. In 1827 he married, and in that year he was made a full professor. In 1833 he succeeded Rudolphi as director of anatomy and physiology, becoming the last to teach that combination of subjects at the University of Berlin.

He almost immediately began to publish accounts of the studies that had occupied his thoughts. Already he had made most valuable investigations into the structure of various glands, their secretions and the lymphatics. For embryology he described what is known as the müllerian duct.

In 1833 appeared a volume, or handbook, of physiology. Müller was then only 32 years of age. The "Handbook" treated only of physiology in general. It contained not only all the facts then known of the science but a discussion of principles, in particular the physiology of nerves and of nerve centers, expounded in a manner not hitherto attempted. By the general use of this great textbook an impetus was given to the investigation of biologic problems by the methods of physical and chemical sciences. The student was forced to wait several years for its sequel, while he learned of the nature of the senses and their special functions.

In the meantime appeared his definition of Bell's law, on the difference in function between the anterior and the posterior spinal nerves, and his conception of reflex nerve action.

Johannes Müller immediately became distinguished by his writings on the physiology of motion, the physiology of fetal life, as observed by dissection of invertebrates, especially articulates, by his contributions to embryology and histology and by his researches on the physiology of the nervous system, on human anatomy and, to some extent, on animal chemistry; moreover, he was interested in ethnology, comparative anatomy of vertebrates, systematic zoology and even paleontology.

JOANNIS MUELLER

DE

RESPIRATIONE FOETUS

COMMENTATIO PHYSIOLOGICA,

IN ACADEMIA BORUSSICA RHENANA

PRAEMIO ORNATA.

Πάντα δοκιμάζοντες, τὸ καλὸν κατέχετε.

CUM TABULA AENEA INCISA.

LIPSIAE,

APUD CAROLUM CNOBLOCHIUM

MDCCCXXXII.

Fig. 2.—Title page of Müller's essay; his handwriting is shown below.

Müller's works contain a vast number of well observed facts. He attempted to solve all problems through speculative philosophy rather than by experimental physiology. Later he visited Goethe at Weimar, and they told each other of their experiences. There was a mystic element in Müller's nature; he assured Goethe that when he was in a state of complete mental repose in a

dark room he could see brilliant figures in his visual field, yet he was not able to call up such figures voluntarily. Goethe, however, declared that he himself could call up whatever he willed. Their discussions covered many topics, but in the end Müller came to the conclusion that while Goethe posssessed the poetic constructive power his own initiative led him in the direction of what was real and physiologic in nature. Despite Müller's unbounded admiration for Goethe, he became aware of the vital difference between Goethe and himself and realized how unstable were such principles that could not present an objective demonstration. Up to about this time Müller was imbued with a distinctively mystic attitude toward the phenomena of existence. At the beginning of the nineteenth century physiologic science was cramped by the speculative

Fig. 3.—Portrait of Johannes Müller, made in 1826.

method of metaphysics, and the fundamental nature of vital action was held generally to be beyond experimental confirmation.

Fortunately at this period the perfection of the microscope led to the revelation of the minute formations of the animal body, and through the establishment of the cell theory by Schleiden and Schwann the conception of the unity of origin of all the tissues of the body came into existence. From then on Müller ceased to be a vitalist. A vitalist was one who regarded the phenomena of life as the result, or property, of the combination of elements together with the existence of an organic, or vital, principle, or force. From his experience Müller was aware of the importance and the effects of physicochemical analysis of organic life, yet he realized that there still remained some force which could not be explained by the analysis. As a histologist he worked out the whole anatomic structure of the glandular and the cartilaginous tissues and grouped the connective tissues, thereby preparing the way for the revelation of his pupil Schwann. His studies in embryology on the müllerian duct and in pathology on the histology of tumors are well known.

From this time on Müller was regarded as the founder of modern physiology. In his teaching and publications he not only summed up the work of his predecessors but instituted methods of experimental and microscopic investigation. He carried out and recorded most valuable observations on the mechanism of sight, hearing and the voice. In connection with these special

HANDBUCH

der

PHYSIOLOGIE DES MENSCHEN

für Vorlesungen

Von

Dr. Johannes Müller.

Ordentl. öffentl. Professor der Anatomie und Physiologie an der Königl. Friedrich Wilhelm-Universität und an der Königl. medicinisch-chirurgischen Militair-Akademie in Berlin, Director des Königl. anatom. Museums und anatom. Theaters, correspondirendem Mitgliede der Kaiserl. Academie der Wissenschaften zu St. Petersburg, Mitgliede der Kaiserl. Leopold. Carol. Academie der Naturforscher, des Vereins für Heilkunde in Preussen, der medicinisch-chirurgischen Gesellschaft zu Berlin, der schwedischen Gesellschaft der Aerzte zu Stockholm, der Gesellschaften für Natur- und Heilkunde zu Heidelberg, zu Erlangen zu Mainz

Ersten Bandes erste Abtheilung.

Mit Königlich Würtembergischen Privilegien

Coblenz

Verlag von J. Hölscher.

1833.

Fig. 4.—Title page of Müller's "Handbook of Physiology of Man."

senses should be included the phenomenon of reflex action. His principal contributions on the senses were his investigations of specific nerve energies and his explanation of color sensations caused by pressure on the globe, which produces on the retina the now well known "pressure phosphenes."

Such I offer as the background for the exposition of the character of a contributor to ophthalmologic science. Repetitions of certain facts have purposely been made to bring them most vividly to immediate attention.

There never was a time when Müller was not interested in the visual powers or responses of the human eye. In early boyhood he used to amuse himself in making out, or fancying that he could see, forms emanating from the cracks and erosions in the plastering of the blank walls of the adjoining house, as he sat at his window. Such subjective visual impressions would remain with him for a variable time, somewhat like "after images," the memory of them remaining indefinitely, although he could not at will revive it. He mused over his experiences, but when he was given Goethe's *"Zur Farbenlehre"* published in 1810, that author's accounts of the phenomena perceived by himself aroused in the lad the desire to understand how they occurred and to meet the great man, who might explain what had been so mysterious.

When Müller went to Berlin he became associated with Seebeck, who for some time had been experimenting with phenomena of color. Together they worked on a series of studies to ascertain the effects of colored lights on vital phenomena. Nothing, however, came of these studies except to increase Müller's wish for the time to come when he might consult Goethe. Yet it was after ten years that Müller actually sought contact with him.

For many years Goethe and his works exerted a marked influence on Müller, which continued irresistibly until a later period in his life, when the student turned from "philosophy" to "fact." In the meantime Müller, who had been recording his own observations, finished in the autumn of 1825 a work on the "Comparative Physiology of the Visual Perceptions of Man and Animals with an Investigation of the Movement of the Eyes and of Human Vision," which he illustrated with numerous charts and tables. This was published in 1826 and immediately attracted the attention of the learned world to the formerly dreamy Johannes Müller. The matter, in part, was taken from Goethe's book, one of the sections being entitled "Fragments on Theories of Color, especially Goethe's 'Theory of Colors.'" Müller sent a copy to Goethe as "the gift of a hitherto silent and unknown follower," together with a letter lauding the "scientific attainments of the Master."

In the same year he published an ingenious essay, "On Fantastic Visual Appearances." In this little volume of one hundred and seventeen pages, he discussed such topics as sight, hallucinations, illusions, visions and imagination. Inevitably, the pursuit of these subjects led Müller unconsciously into the deepest psychologic experimentations, and his contemplation of the results which he obtained rounded out the subjective phase of his life and irresistibly caused him, in his sincere search for the truth, to delve deeper and deeper into human physiologic investigation, hoping thereby to verify the mystic and subjective aspirations which had animated him. The outcome was the preparation of a manual, or handbook, of physiology, which appeared in 1833.

The "Handbook," as issued in 1833, dealt only with physiology in general. The long-awaited second volume, which included a discussion of the senses, appeared in 1840. It is this division of the "Handbook" which should be of special interest, as it told what was then known about vision. A perusal of the work will lead one to regard this early exposition of the reactions of the several senses as a foundation of modern experimental psychology, as in it were indicated the bases of the responses of the various sense organs to external stimuli. He showed

Zur vergleichenden

Physiologie des Gesichtssinnes

des Menschen und der Thiere

nebst

einem Versuch über

die Bewegungen der Augen

und über

den menschlichen Blick

von

Dr. Johannes Müller,

Privatlehrer der Medicin an der Universität zu Bonn, praktischem Arzte und Wundarzte daselbst, Mitglied der Kaiserl. Leopoldin. Carolin. Academie der Naturforscher.

Leipzig,

bei C. Cnoblech.

1826.

Fig. 5.—Title page of Müller's "Comparative Physiology of the Visual Perceptions of Man and Animals with an Investigation of the Movement of the Eyes and of Human Vision," published in 1833.

that in whatever way a terminal organ is stimulated the result is the same in consciousness, according to the nature of that particular organ. He recorded that when the retina is stimulated by light, electricity, heat or mechanical pressure, as by a blow, the response will always be the same, namely, the sensation of flashes of light, possibly of color. Further, the same response will follow any kind of irritation of the optic

Ueber die

phantaſtiſchen

Geſichts-erſcheinungen.

Eine phyſiologiſche Unterſuchung

mit einer phyſiologiſchen Urkunde des Ariſtoteles über den Traum,

den Philoſophen und Aerzten gewidmet

von

Dr. Johannes Müller,

außerordentlichem Profeſſor der Medicin an der Univerſität in Bonn, practiſchem Arzte und Wundarzte daſelbſt, Mitglied der Kaiſerl. Leopoldin. Carolin. Academie der Naturforſcher.

MAY 26 1902

Coblenz,

bei Jacob Hölſcher.

1826.

Fig. 6.—Title page of Müller's "On Fantastic Visual Appearances," published in 1826.

nerves, which convey impulses from the retinas to the brain. From these reactions Müller deduced the great law of the "Specific Sensibility of Nerves," by which he meant that each nerve of a special sense has its own sensibility. As Clarke Maxwell later pointed out: "It was a great step to recognize that the sensation due to a particular nerve may vary in intensity, but not in quality."

It is of interest to know how Müller divided his classifications of vision. After considering the physical conditions, such as the form of the ocular globes, which are necessary to effect the formation of luminous images and which affect and modify refraction and the adjustment of the eyes for the reception of colored rays, he gave an account of the eye as an optical instrument and described the eyes of lower animals. He then enunciated certain theories which he had deduced from a knowledge of the structure of the eye.

Next was described the "adaptation of the eyes for sight at different distances." Not yet had he specifically used the term "accommodation." "Myopia" and "presbyopia" and the correction of these defects by the use of glasses were next discussed. He held the belief that shortsightedness was acquired by habitually using the eyes for the perception of near objects only and that the wearing of spectacles was injurious since they prevented adjustment of the eyes for distinct vision at different distances.

A brief chapter was concerned with the chromatic and achromatic properties of the eye. The final chapter told of the action of the retina, the optic nerves and the sensorium of the eye. It is here that he dwelt on the reciprocal action of the different parts of the retina. Another chapter described at some length simultaneous action of the two eyes, single vision with two eyes, cause of single vision and phenomena and causes of double vision. Singularly, Müller regarded the macular region, the "central foramen" of the retina, as of no vital importance. It must be borne in mind that there was no ophthalmoscope at that period. The section ends with the subjective phenomena of vision, in which he specified defective color sense and referred to the existence of objects within the eye which interfere with vision but do not necessarily lead to amaurosis. Müller had been subject to muscae volitantes since childhood. For the elucidation of many of the statements on these topics, one must look to his earlier treatise on the physiology of vision.

As early as 1826 Müller had tabulated the results of his investigation of the sight in unbalanced strabismic eyes, grouping the defect in several classes, including strabismus associated with amblyopia, strabismus caused by oculomotor paresis and strabismus caused by myopia.

I shall refer particularly to the type which he described as "strabismus incongruus." He was greatly handicapped by a lack of understanding of the facts, so well understood today, of the errors of refraction, with which strabismic eyes were noted, even then, to be not uncommonly associated. His "strabismus incongruus" was deemed by Donders to be an "apparent strabismus." Müller had no regard for what

was later considered as the relative positions of the two "yellow spots." He became confused when the muscular anomaly was not present at every examination, for he had noticed that it was possible for the subject temporarily to overcome the muscular aberration. Nevertheless, he took advantage of these observations to confirm the facts connected with the "identical points."

Müller, however, recognized that a connection existed between convergence of the visual lines and adjustment of the eye for different distances. He assumed that the connection is absolute and that a definite convergence is necessarily attended by a definite adaptive power; beyond the limits of accommodation a greater or less convergence is possible, the accommodation corresponding to the nearest and the farthest point of distinct vision. He graphically noted that persons with pronounced myopia commonly looked at near objects with one eye, and at distant objects with the other, equally nearsighted, though seeing indistinctly, if at all. That condition, in all its aspects, Donders later spoke of as "relative divergent strabismus."

Fig. 7.—Portrait of Müller, made in 1837.

Of truly greatest value was Müller's comprehension of binocular single vision. He observed, entirely theoretically, in his studies of ocular movements in the normal patient, whose eyes were balanced one with the other, that the movements of the eyes would always cause the images to fall directly on corresponding parts of the two retinas, producing single vision. And, on the contrary, if from various causes the images fell on noncorresponding points, double vision resulted; that is to say, the patient saw two objects instead of one. The pairs of "points" giving rise to single vision he termed, as already mentioned, "corresponding points." He assumed that single vision was effected by the passage of similar fibers from these points to the brain, which became united and gave rise to the consciousness of a single object.

It is well known that for centuries it was believed, by Müller and others, that one eye was used at a time, that one remained relaxed and inattentive to objects while the other was on the stretch, and also that single vision was obtained by the union of the two optic nerves before they reached the brain. It is true, moreover, that as far back as the Dark Ages the Arabians had observed many of the reactions which Müller described from the results of his independent studies. Hunain, in the ninth century, described single vision being effected when the corresponding points are disturbed, and Alhazen, too, wrote about "two corresponding points of the retina, the mind perceiving but one image."

Müller must have had an attractive personality, as evidenced not only by his success as a lecturer and the charm of his style but by the scientific ardor and interest which he inspired to a degree and continuously sustained in his audience. He awakened in them new ideas, evoking a stimulation with which to search for further proof of his teachings.

He was a true teacher, whose lectures from the beginning were regarded as the best at the University. By the tact and dignity of his manner during anatomic demonstrations and by the accuracy and completeness of his teaching, Müller, although he was not particularly eloquent, drew large crowds and enlisted a greater number of students than was ever before recorded. He was distinguished for the rapidity and accuracy with which he made his observations, and, being a gifted draughtsman, he easily illustrated his topic, step by step, on the blackboard. While he was an impressive teacher, influencing and inspiring his pupils for good, as only a great man can, and popular with the large numbers who attended his public lectures, he carefully chose only a select group of pupils for a more intimate association with himself. They profited by their contact with him and became in after years famous in their special subjects, which had been initiated and inspired by Johannes Müller. So deeply penetrative was their master's teaching that in their subsequent works may be traced the origin of the main current of modern medicine; indeed even through what they later taught may be seen who laid the foundation of our present beliefs and by whose researches into the

domains of experimental science the mere speculative metaphysics so prevalent early in the last century became dispelled.

Besides the histologist Schwann, of special interest should be mentioned that genius Virchow, the physiologist DuBois-Reymond, Helmholtz, Brücke and the incomparable von Graefe, all of whom must be accorded places in the front ranks of medical science throughout the ages.

In so short a working life, few have accomplished more than did Müller. It is impossible for me to give anything approaching the consecutive details of his scientific labors or literary productiveness. The number of his independent works amounts to twenty; of his lesser treatises and essays there are two hundred and fifty. In thirty-seven years he published, one year after another, every seven weeks, a scientific dissertation of from three to five printed sheets, illustrated by from one to three plates drawn by himself. The number of positive facts on different subjects which he brought to light, if not original with him, surpasses representation. In 1834, he began the *Archiv für Anatomie und Physiologie*, which has been continued by his successors ever since, familiarly known as *Müller's Archives*.

Fig. 8.—Johannes Müller at about 30 years of age.

At first his experimentations were frequently rough and lacked balance, but it was his rule to investigate over and over again until he was satisfied and then to publish his result. He was fearless in research, strikingly accurate in his results and never ashamed to confess his ignorance. He was gifted with a remarkable memory, so powerful that once a fact was acquired it was remembered forever.

Fig. 9.—Portrait of Müller, made in 1857 (from a photograph), expressive of physical anxiety in the last years of his life.

If it has been declared that Müller, in spite of his greatness, did not make any discovery in ophthalmology of the highest rank, it must be admitted that he investigated and turned to the best account what others had discovered. It remained for Müller to extend and verify what others might not fully have demonstrated. As a histologist his studies of various tissues led Schleiden and Schwann to establish the cell theory. He was one of the first to employ the microscope in studies of pathology. To students of the history of anatomy and physiology, his name is familiar, for he stood forth as the great champion of induction in the investigation of

nature. His observations in comparative anatomy are most valuable, especially as they concern the visual organs of the lower animals.

As a morphologist he carried on investigations of the first rank of the structural relations of the ganoid and other rare and fast disappearing fishes as well as of additional marine forms.

A bound catalog of Müller's library is at the College of Physicians of Philadelphia. And what a library it must have been! Rarely has such a collection been made by one person. Besides what he himself purchased it contained many valuable presents from all parts of the world.

Müller was of medium stature, strongly built, with broad shoulders and a massive head. In his youth he was graceful and slender; in later life, extremely corpulent. His manner was simple. He was never ill, was never exhausted and appeared to have been gifted with eternal youth. But, alas, in his studies on the sense of vision, his observations were conducted so unceasingly that his eyes were injuriously affected, so that his later studies were carried on only with increased difficulty. In his early days and until about 1850, he boasted that he could sleep at any moment he wished. In his last years sleeplessness troubled him, and for relief of it and of pain in his abdomen he took large doses of opium. After a while his spirit changed, and he became restless and anxious. Toward the Easter of 1858, while preparing for a holiday along the Rhine, he broke down completely. As the summer term approached he resigned his chair at the University and prepared for a consultation, but on April 26 he was found dead in his bed, having put himself to his final sleep.

I trust that I have been able to do justice to the subject and have pointed out that Müller was somewhat more than only a fellow worker with and a friend of Helmholtz, as indicated in the sketch of Müller in "The American Encyclopedia of Ophthalmology." And I suggest consultation of his original works, copies of which I, regretfully, do not possess. As all were published by 1840, librarians refuse to allow them out of the libraries.

If the world had forgotten Müller at the close of his life, the accounts of the man and his works written as a labor of love by Virchow and those by DuBois-Reymond would lead one to think well of him.

Long after Müller's death Helmholtz wrote: "When one comes into contact with a man of the first rank, his spiritual scale is changed for life. Such a contact is the most interesting event that life can offer."[1] And I would add the words of "Pompilia," by Robert Browning:

> Through such souls alone
> God stooping shows sufficient of His Light
> For us in the dark to rise by.

317 South Fifteenth Street.

1. McKendrick, J. G.: Hermann Ludwig Ferdinand von Helmholtz, London, T. F. Unwin, 1899, p. 14.

SPONTANEOUS RETINAL REATTACHMENT

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The course of serous retinal detachment is sometimes curiously modified when the detachment of the retina remains stationary and there is reattachment, which gives rise to a characteristic ophthalmoscopic picture. This condition is observed in a small percentage of cases, and only when the detachment occupies the lower half of the eyeground. The detachment is shallow, and its upper boundary is bound down by chorioretinal changes, which constitute the most striking sign. The retina in the course of time becomes reattached except for small areas in the extreme periphery, where there are one or more holes or an area of dialysis. The reattached, flat retina is generally changed to a paler, yellow gray; there are characteristic branching white subretinal lines and areas where the choroidal markings are more distinct and irregular retinal pigmentation is present. The upper boundary consists of organized exudate, which extends across the fundus below the disk in a curved or in a more or less straight line to the periphery on each side and divides the fundus into two dissimilar parts. This boundary limits the extent of the detachment unless the limiting line does not extend clear to the periphery; then a new detachment may subsequently develop, as occurred in 1 of my cases. The boundary consists of white bands or streaks of organized exudate with a deal of black pigment, or both changes may be present. The detached area in some cases includes the macular region; the macula then presents cystic changes which resemble a hole, and the ophthalmoscopic picture is that characteristic of a shallow detachment.

A number of histologic examinations have been made. Leber [1] described white branching lines after reattachment of the retina and expressed the opinion that they were due to the coagulated fibrin in the subretinal fluid and subsequently were transformed into connective tissue. These lines were situated under the retinal vessels and always indicated a previous detachment; they were quite different from retinal folds. Müglich [2] spoke of a fine, fibrillated mass with few nuclei, internal to the pigment epithelium, to which connective tissue bands from the choroid and retina were attached and were surrounded by clumps of pigment. There were also thick connective tissue bands in the external fiber layers of the retina. Rönne,[3] in an anatomic specimen, noted a limiting band between the degenerated and the normal portion of the retina in the form of a partially pigmented wall of connective tissue. The ophthalmoscopic picture of spontaneous reattachment is well illustrated in Müglich's [2] article and in Oeller's "Atlas." [4]

I have observed 18 cases in which reattachment of the retina had taken place. The detachment was always old, and the onset dated back a number of years. In 1 case in which the history was of shorter duration the macular involvement was probably recent, while the detachment was definitely old, to judge by the appearance of the region around the hole in the periphery of the retina. As this type of detachment always occurs in the lower half of the fundus, the association with dialysis is not strange. In other cases one or more holes were present in the periphery of the retina. Of the cases which are the basis of this paper, areas of dialysis were present in 6 and peripheral holes in 5, and no hole was seen in 7 cases.

SUMMARY OF CASES

CASE 1.—E. K., aged 26, had onset of retinal detachment at least three and a half years prior to consultation. Vision in the right eye was 2/200. The detached area extended from 5 to 9:30 o'clock, with a boundary of chorioretinal changes reaching up to the disk and including the macula. Branching lines and pigment were noted; holes were noted in the periphery.

CASE 2.—R. B., aged 55, had vision of 20/20 in the right eye. Detachment, of ten years' duration, was present in the lower half of the eyeground, from 5 to

Read at the Eightieth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., May 30, 1944.

1. Leber, T., in Graefe, A., and Saemisch, T.: Handbuch der gesammten Augenheilkunde, ed. 2, Leipzig, W. Engelmann, 1916, vol. 7, pt. 2, p. 1442.

2. Müglich, G. T.: Ueber Spontanheilung der Netzhautablösung, Inaug. Dissert., Marburg, F. Sömmering, 1891.

3. Rönne, H.: Zur Anatomie der Streifenbildung nach Netzhautabhebung, Arch. f. Ophth. **71**:284, 1910.

4. Oeller, J. N.: Atlas seltener ophthalmoskopischer Befunde; Zugleich Ergänzungstafeln zu dem Atlas der Ophthalmoskopie, Wiesbaden, J. F. Bergmann, 1904, plate XIII, fig. 23.

8 o'clock, and was firmly delimited; it did not include the macula. Retinal atrophy, pigmentation and white lines were present. There was a tear of the ora serrata.

CASE 3.—S. R., aged 29, had sustained an injury eight years before consultation. Vision in the right eye was 15/200. An area of detachment extended from 4 to 8 o'clock. A well marked chorioretinal boundary extended to the disk and included the macula. White lines and choroidal changes were present (fig. 1). In the lower outer portion of the periphery there was a suspicious area of pathologic change in the retina.

CASE 4.—J. B., aged 23, had had poor vision for twelve years. Vision was 20/70 in the right eye. A healed area of detachment extended from 6 to 9 o'clock and skirted the macula. There were white lines and pigmentation at the upper margin. No holes were seen.

CASE 5.—E. K., aged 41, had vision of 3/200 in the left eye. There had been failing vision for many years. An area of detachment extended from 3 to 8 o'clock, with a margin of white lines passing horizontally through the macular region. No hole was discovered.

to 7 o'clock and was sharply outlined at some distance from the macula. Three holes were noted in the periphery at about 4:30 o'clock.

CASE 9.—G. P., aged 36, had had failing vision for sixteen years. Vision was 6/200 in the right eye and 2/200 in the left eye. Retinal detachment was present in both eyes, with a nearly horizontal chorioretinal boundary and involvement of the macular region. The latter presented cystic changes. No hole was discovered.

CASE 10.—L. G., aged 45, had had poor vision for four years; vision in the left eye was 5/200. An area of detachment extended from 3 to 7 o'clock, with a chorioretinal outline, especially in the nasal portion. The macula presented cystic changes. A hole was noted in the extreme temporal part of the periphery.

CASE 11.—R. G., aged 22, had discovered failing vision in the right eye by chance one month before he was seen. Vision in that eye was 20/30. The history was uncertain. A detachment, from 3 to 8 o'clock, was

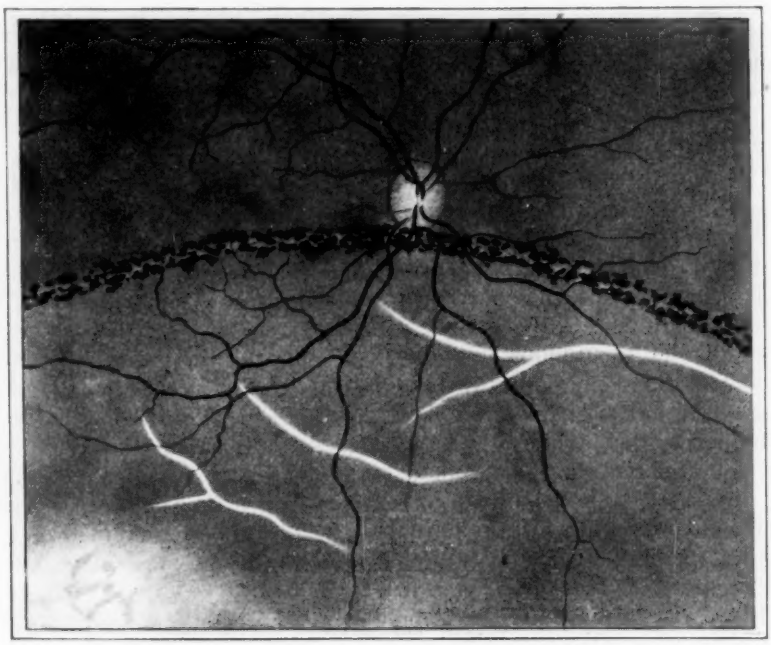

Fig. 1.—Drawing showing the organized boundary and wavy white lines in the reattached retina.

CASE 6.—F. B. C., aged 16, had vision of 8/200 in the left eye. Failing vision was discovered by chance two years prior to consultation. An area of detachment, from 2:30 to 8 o'clock, included the macula and had a sharp chorioretinal outline; an area of dialysis was noted at 5 o'clock.

CASE 7.—J. B., aged 37, had noted poor vision in the right eye for fourteen years and in the left eye for one and a half years. Vision in the right eye was limited to perception of hand movements and was 10/200 in the left eye. There was an area of detachment in the lower fields of both eyes. The detachment extended from 5 to 9 o'clock in the right eye and from 3 to 8 o'clock in the left eye, with an outline of pigmented and choroidal changes. Holes were present in the lower and outer part of the periphery.

CASE 8.—J. K., aged 22, had vision of 20/20 in the left eye. An area of detachment extended from 2:30 well delimited by white lines. There was a tear in the ora serrata at 7 o'clock.

CASE 12.—E. E., aged 69, had had poor vision for five years. After cataract extraction vision in the left eye was 20/100. There was a typically outlined reattachment of the retina, extending from 3.30 to 9 o'clock, which was undoubtedly old. No hole was visible, though suspicious changes were present in the temporal portion of the periphery.

CASE 13.—R. P., aged 23, had first noted loss of vision two months before. Vision in the right eye was 20/200. There was a shallow detachment from 3 to 8 o'clock, which was outlined with beginning changes. A tear was present in the ora serrata.

CASE 14.—J. S., aged 69, had vision of 10/200 in the right eye and of 20/20 in the left eye. Failing sight was noted in the right eye two months before admission; then, an old condition was discovered in the left

eye. The left eye presented an area of reattachment of the retina in the lower half of the fundus, extending from 4 to 8 o'clock, with a pigmented margin at some distance from the disk and the macula and with several holes in the periphery of the retina below. An area of detachment was present in the lower part of the eyeground of the right eye, without defined outline but with changes and holes in the retina.

CASE 15.—M. S., aged 16, complained of failing vision in the left eye two years prior to admission. Vision at the time of examination was 5/200. An area of reattachment in the lower outer portion of the fundus, from 3 to 7 o'clock, included the macula, with a white-lined limiting margin; subretinal white lines and choroidal changes were present. There was a tear in the ora serrata, with a surrounding shallow detachment at 5 o'clock (fig. 2).

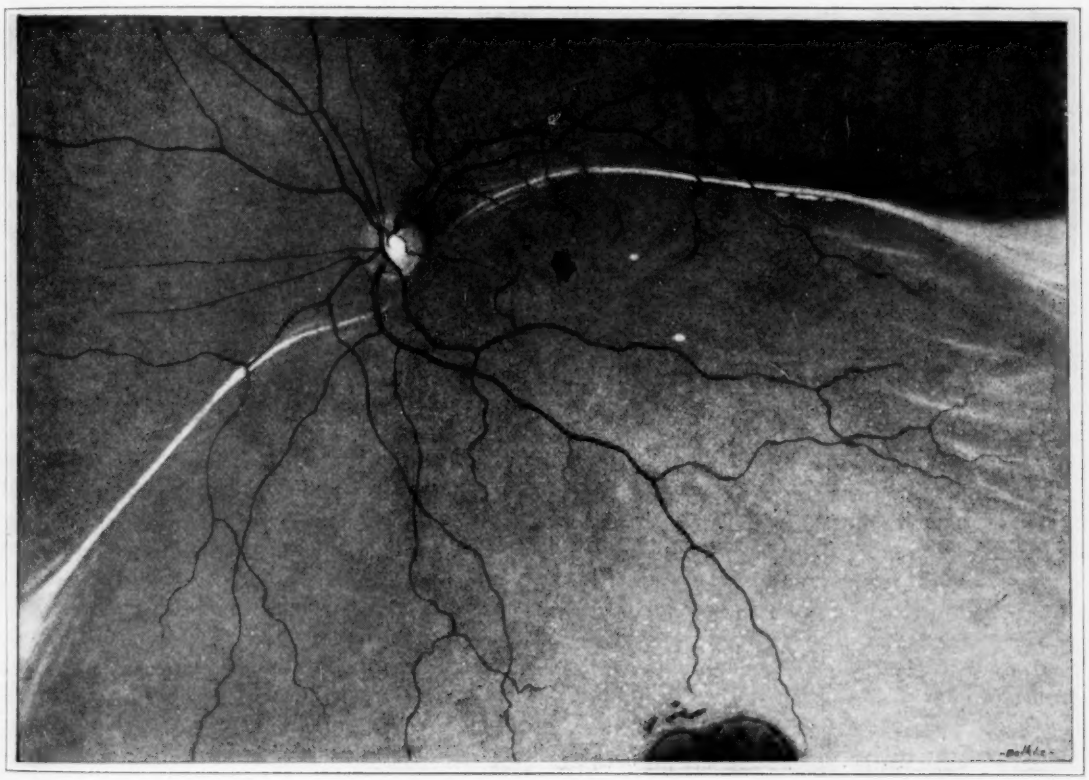

Fig. 2.—Drawing showing white lines at the upper boundary in a case of reattached retina with dialysis.

CASE 16.—R. P. R., aged 45, had injured the right eye with a baseball at the age of 12. Sight had remained stationary until four weeks prior to consultation. At the time of examination vision in the right eye was 20/30. An area of healed detachment was shut off by a line of adhesive choroiditis, extending from 6 to 9 o'clock. This limiting line stopped short in the temporal field, and a recent detachment extended upward and centrally. An area of dialysis was present at 7 o'clock.

COMMENT

In these cases the detachment was stationary if the limiting line went clear to the periphery. The field defect which corresponded to the extent of the old detachment remained unchanged. Preservation of central vision depended on involvement of the macular region. In 5 of the cases central vision was practically normal, and in 1 of these cases the detachment was not noticed until the other eye became affected.

A detachment limited to the lower part of the field which is not an extension of a detachment in the upper part of the field is generally shallow and is usually caused by a hole in the periphery of the retina. Either such a hole is round and comparatively small, or a dialysis is present. The large crescentic, or horseshoe, tear so frequently present in the equatorial region with detachments in the upper part of the field does not occur with detachments limited to the lower portion of the eyeground. The present accepted explanation of the cause of retinal detachment assumes the presence of degenerative changes in the retina and in the vitreous body, with the formation of an adhesion between these two structures. This adhesion results in a tear of the retina due to rotatory movements of the vitreous body. This does not explain the causation of the detachment in the cases just described. First, these detachments occur in young people, in whom degenerative changes are not frequent, and in the case of a dialysis the cause is entirely physical. Moreover, the adhesion of the vitreous to the under-

lying retina in the periphery of the eyeground is normally unusually strong, so that a pathologic process which binds the vitreous and the retina together need not be present. It is possible that the firmer texture of the vitreous body, at its base, as Salzmann called it, may explain why the escape of the vitreous fluid in this type of detachment is moderate. Finally, an important factor in the shallowness of a detachment limited to the lower half of the eyeground may be the weight of the vitreous body, which acts most on the lower half of the fundus.

The question of operation in cases of reattachment of the retina is of practical importance. The field defect cannot be restored by late operation; it remains stationary and permanent. Central vision depends on involvement of the macula. The only object of an operation in a case of late detachment is to preserve the macular area if it is not firmly shut off, and the feasibility of this operation depends on the extent and the age of the macular change. Notwithstnding the prospect of self limitation of a retinal detachment which is limited to the lower half of the fundus, an early operation should be performed to avoid involvement of the macula and to preserve the visual field.

10 East Fifty-Fourth Street.

REMOVAL OF THE RUPTURED CAPSULE IN OPERATIONS FOR CATARACT

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The capsule sometimes ruptures in the so-called intracapsular operation for cataract, no matter what method is employed. If the broken capsule recedes into the eye most operators make no attempt to remove it, the operation becoming an unintentional extracapsular extraction. If the cataract is immature, as it usually is, a considerable amount of lens matter also remains in the eye in spite of irrigation, and there often result posterior synechias in addition to secondary cataract. Frequently discission is later necessary before satisfactory vision is obtained, and sometimes iridotomy is required. In some cases the retained lens matter causes phacoanaphylactic endophthalmitis. For these reasons I have usually endeavored at the original operation to remove the ruptured capsule with its enclosed lens matter. In 1927 I described methods [1] for doing this, but I am not aware that any one else has even discussed the problem.

With the method of intracapsular extraction [1] that for the past eighteen years I have routinely employed for patients over 45 years of age, rupture of the capsule seldom occurs. In this technic, which is often called "the sliding method," the capsule is grasped with a forceps at or near the upper margin of the lens. When rupture does occur, it is obviously due to one or more of the following causes: 1. Imperfect technic: The incision is too small for the cataract, or, more often, the operator through impatience exerts too great traction with the forceps or too little pressure with the expresser.[2] 2. The forceps is poorly adjusted and tends to bite a hole in the capsule. 3. The patient is a "bad actor," making a wide movement of the eye at a critical time. With the "sliding method" the danger from this cause is less than with methods in which the capsule is grasped within or below the pupillary area. I have found that my patients have been more cooperative in recent years, a fact which I attribute chiefly to their increased confidence in an older operator. 4. The cataract is so thin or so small that pressure on the cornea is of relatively slight assistance in dislocating the cataract and forcing it out of the eye, so that the cataract must be removed chiefly by traction. 5. The vitreous is so fluid that pressure on the cornea is ineffective. 6. The eye is highly myopic, the large size of the vitreous chamber, along with some fluidity of the vitreous, decreasing the effectiveness of pressure on the cornea. However, although I have found intracapsular extraction in cases of high myopia difficult, I have seldom ruptured the capsule in such cases. Possibly this is because the zonule is likley to be relatively weak in highly myopic eyes. 7. The capsule is unusually fragile. 8. The zonule is unusually resistant. In exceptional cases it is so resistant that it is impossible to dislocate the cataract by any method I have deemed safe.

There are two types of rupture of the capsule that are really fortunate occurrences, for each not only insures complete removal of the capsule but as concerns loss of vitreous makes the operation safer than when the cataract is removed intact. In one of these types the capsule ruptures below and is completely removed by the forceps, the cataract being left within the eye. To avoid rupturing the hyaloid membrane, the nucleus should then be expressed with great care, and the sutures should be pulled up before the remaining lens matter is irrigated out. In the other type the capsule ruptures elsewhere but remains prolapsed in the wound after the nucleus has been expressed. In cases of this type the capsule can easily be picked up with a forceps and completely removed. It is safer to tie one or both sutures before this is done. Neither of these types of rupture is frequent; the second occurs much more often than the first.

Most often, however, when the capsule ruptures it does so at or near the grasp of the forceps. Occasionally only a small hole is produced here, and the capsule can be regrasped near the hole and the operation continued in the usual way. But usually when the capsule ruptures above it retracts into the anterior chamber. In cases of this kind I introduce the capsule forceps on the flat into the eye as deeply as necessary and

Read before the American Ophthalmological Society, Hot Springs, Va., May 29, 1944.

1. Verhoeff, F. H.: A New Method for Removing Cataracts with Their Capsules, Tr. Am. Ophth. Soc. **25**:54, 1927.

2. Verhoeff, F. H.: Lens Expresser, Tr. Am. Ophth. Soc. **28**:305, 1930.

attempt to grasp the capsule by pushing one blade into the cataract beneath the capsule and the other blade between the capsule and the cornea. If this maneuver is successful the cataract and all of the capsule can usually be removed by traction with the forceps and pressure on the cornea.

In many cases, when the ruptured capsule has receded all attempts to regrasp it fail while the cataract is still within the eye. In such cases, when this procedure seemed not too hazardous, after first expressing the cataract, tying one suture and employing free irrigation, I have attempted to grasp the capsule with my angular capsule forceps. The forceps was introduced on the flat, one blade being passed behind and the other in front of an edge of the broken anterior capsule. Many times I have succeeded in this way in removing the entire capsule without loss of vitreous. However, since the anterior chamber is obliterated, the iris hinders the introduction of the forceps, and one blade must be rubbed against the cornea while the other pushes back the delicate posterior capsule and the hyaloid membrane. As a result, the hyaloid membrane may be ruptured, and loss of vitreous may occur. To obviate this danger and at the same time to facilitate the introduction of the forceps into the pupillary area, I devised about two years ago a simple procedure that has proved eminently satisfactory. It converts what would have been a more or less unsuccessful operation into a highly successful one. With this to fall back on, rupture of the capsule in cases in which there is great danger of loss of vitreous may be a blessing in disguise. To present this procedure is the chief purpose of the present communication.

The procedure consists essentially in keeping the anterior chamber filled while the capsule is grasped and removed with the angular capsule forceps. After one suture has been tied the opening of the wound is so much reduced in size that the chamber can easily be kept sufficiently distended by gentle, continuous irrigation with isotonic solution of sodium chloride. For the irrigation a small metal tip attached to a rubber bulb is used. Occasionally I have carried out the irrigation with my right hand while I removed the capsule with a forceps held in my left. I prefer, however, that a capable assistant carry out the irrigation. Then I can give my entire attention to the delicate task of removing the capsule and, moreover, can use my right hand for this purpose.

As a rule, when the entire chamber is kept filled and strong illumination is used, an edge of the ruptured capsule can be seen in the pupillary area and this edge can be quickly grasped. Sometimes it is impossible certainly to distinguish capsule from cortical matter. In this event several attempts may be necessary before the capsule is grasped. After it is grasped the entire capsule can generally be removed by gentle traction with the forceps. Occasionally when the capsule is partly out of the wound it begins to tear at or near the grasp of the forceps. Then I employ what I call a hand over hand maneuver. With a fixation forceps or another capsule forceps held in my left hand, I grasp the capsule close to the wound, pull it out a short distance and grasp it again near the wound with the forceps in my right hand. This process is repeated until the capsule is completely removed. Usually the capsule brings out, enclosed within it, a surprising amount of lens matter. Only in exceptional cases is the capsule so firmly attached to the zonule that but a small part of the capsule can be torn away. Even in these cases, however, the procedure is worth while, since a hole is left in the anterior capsule in the pupillary area. These are the cases previously referred to in which safe removal of the cataract in its capsule is impossible. Some operators fear that severe traction on the zonule may cause serious cyclitis. No doubt this fear is based chiefly on theoretic considerations, for it is not justified by my own actual experience.

If the patients are sufficiently cooperative, this procedure can and in my opinion should be carried out also in intentional extracapsular extractions, including linear extractions. I assume, of course, that if the iris is adherent to the capsule it has been freed by a spatula before the capsulotomy. Instead of attempting intracapsular extraction in certain otherwise uncomplicated cases of senile cataract in which I especially feared loss of vitreous, I have been tempted deliberately to cut the capsule above and then to employ this procedure. However, because I seldom break the capsule or lose vitreous even in such cases, I have never yielded to this temptation. I have also planned but not yet tried several other procedures for removing a cataract and its capsule separately. One of these is to grasp the lens above as usual, cut the capsule within the pupil with a cystotome, express the nucleus while retaining hold of the capsule and then remove the capsule by traction with the forceps, tie one or both sutures and finally employ irrigation if necessary.

Sutures are especially important, perhaps essential, for the success of the procedure. In a case of linear extraction I employ only a single suture, but in a case of senile cataract I use always two and sometimes three corneoscler-

conjunctival sutures such as I described in 1927.[3] In Beetham's modification[4] of my operation I have found three sutures necessary to insure against prolapse of iris. This modification consists in removing the cataract through an iridodialysis, and I reserve this technic for patients under 50 years of age. Several operators have attempted to improve on my methods of suturing, using procedures that I had long before discarded as inferior.

Years ago I abandoned attempts to remove a cataract in its capsule through an intact pupil, because I became convinced that the resistance of the sphincter too greatly increased the danger of rupturing the capsule. However, I never do an iridectomy in operations for cataract. Instead, I perform a vertical iridotomy through the sphincter to the base of the iris by means of straight scissors. In this way I obtain a small pupil and a small coloboma. When there is glaucoma or suspicion of it I tear away some of the root of the iris in addition.

The capsule forceps I employ for removing broken capsules is the angular forceps[5] described in 1916 for intracapsular extraction. This is the foreceps I used ten years later for the "sliding method." About 1928, however, I modified this forceps[6] so as to make it especially suitable for the "sliding method." This modified forceps is straight, and its biting ends are somewhat different from those of the angular forceps. Because it opens the wound so widely it is not well suited for removing a broken capsule that has receded into the eye. For this particular purpose a forceps still better than my angular forceps could no doubt be devised. As a matter of fact, about twenty-seven years ago I devised for evulsing secondary cataracts a special forceps that may prove an ideal instrument for the procedure under discussion. This forceps is straight and has a cylindric handle which readily permits the capsule to be rolled up on the blades and thus held much more firmly. The blades are long, thin and narrow, so that they do not too greatly distend the cataract incision, and there is a stop to prevent them from opening too widely.[7]

When received from the maker, a capsule forceps is seldom perfectly adjusted. The usual faults are that the tips come together unevenly or pinch the capsule too severely. Every operator should learn how to adjust the forceps by means of optician's pliers. With proper adjustment it is possible to change the grasp of the forceps to another place without causing rupture of the capsule at the original grasp. Not infrequently it is advantageous to do this in order to facilitate the removal of the cataract or to prevent loss of vitreous.

For the irrigation a large container connected to the metal tip by a long rubber tube might be superior to the rubber bulb that I now use. Such an apparatus has been commonly employed for irrigating the anterior chamber, and years ago I routinely employed it. The rate of flow and pressure can be regulated by the height at which the container is held and also by squeezing the rubber tube. However, in the hands of a capable assistant I have found the rubber bulb satisfactory and more convenient. The fluid used is half-strength isotonic solution of sodium chloride. I began to use this for irrigation about twenty years ago, at the suggestion of Dr. Robert Reese, because he had found that after its use less striped keratitis occurred than after the use of full strength isotonic solution of sodium chloride. For distending the anterior chamber while the capsule is being removed perhaps air would be better than fluid, but I have not yet determined this to be a fact.

In especially unfortunate cases of cataract extraction not only does the capsule rupture but vitreous is lost, and a large amount of lens matter is left in the eye. In these cases, since the anterior chamber is already distended, even though it is with vitreous, irrigation would be of no assistance in removal of the capsule and might wash out vitreous instead of or along with the lens matter. In the few cases of this kind that I have had since 1927 I have tied both sutures, introduced the angular forceps between the sutures and then grasped and removed the capsule together with a considerable amount of the lens matter. This procedure entailed a slight additional loss of vitreous, but I regarded this loss as preferable to leaving the capsule and a large amount of lens matter in the eye. Such cases emphasize the value of sutures, for without them the probable additional loss of vitreous would be too great to warrant removing the capsule.

3. Verhoeff, F. H.: A Corneo-Sclero-Conjunctival Suture in Operations for Cataract, Tr. Am. Ophth. Soc. **25**:48, 1927.

4. Beetham, W. P.: Cataract Extraction with Iridodialysis, Tr. Am. Ophth. Soc. **39**:104, 1941.

5. Verhoeff, F. H.: Improved Capsule Forceps for Intracapsular Cataract Extraction, Arch. Ophth. **45**: 479, 1916.

6. I have never published a description of this forceps, but about ten years ago it was described and put on the market by the Storz Instrument Company of St. Louis, from whom it can now be obtained.

7. This forceps is no longer on the market, the firm which originally made it having abandoned the manufacture of ocular instruments.

MITOTIC AND WOUND-HEALING ACTIVITIES OF THE CORNEAL EPITHELIUM

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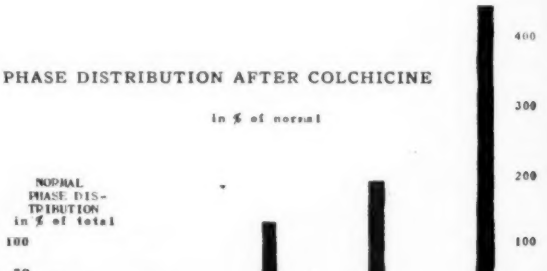
BALTIMORE

This investigation was undertaken in an effort to discover the physiologic controls and biochemical aspects of mitotic and wound-healing activities. Some phases of the work have previously been published.[1] In the present paper we wish to present the general plan of our study and to outline the results so far achieved. These results constitute still a most incomplete survey of the field, and the work is continuing. By physiologic controls we mean the neural and humoral mechanisms by which other tissues and organs influence the mitotic and wound-healing activities of the cornea. Among the biochemical aspects on which we are seeking to obtain light are metabolic processes involved in the mitotic and wound-healing activities.

MITOTIC ACTIVITY

Method of Assay.—A detailed analysis of the method of assaying mitotic activity has been published elsewhere.[1a] Routine counts are made on a meridional strip of the rat cornea, covering an area representing one fiftieth of the whole cornea. Mitoses are noted only in the basal layers of the epithelium and are more numerous near the limbus than at the center. In normal young adult rats (weighing 100 to 200 Gm.) there are approximately 5,000 to 6,000 mitoses per cornea, or 100 mitoses per strip counted. Normal variations range from 50 to 200 mitoses per strip. However, mitotic activity cannot be gaged solely by the number of mitoses present at a single moment, since that number is affected both by the rate at which cells enter mitosis and by the rate at which cells pass through the mitotic cycle. In analysis of the rate of mitosis, as distinguished from the number of mitotic figures, the drug colchicine has proved most useful. Other investigators have shown in other organs that colchicine arrests the mitotic cycle in metaphase but does not, in appropriate dosage, influence the rate at which cells enter mitosis. We have found the effects of colchicine on the corneal epithelium to be of the same kind.[1a] Hence the number of cells observed in mitosis at a fixed time after administration of colchicine furnishes a measure of the rate at which cells enter mitosis.



Normal phase distribution of mitoses in the rat cornea (left) and phase distribution of mitoses after administration of colchicine (right).[1a] In these graphs, *P* indicates prophase; *M*, metaphase; *A*, anaphase; *R*, reconstruction phase, and *T*, telophase.

In addition, it is possible to make differential counts of the number of cells in the various phases of mitosis. The usefulness of this procedure can be seen in the figure, which presents the results of phase counts at various intervals after the administration of colchicine. It will be seen that, except for a slight drop during the first hour after the intramuscular injection of this drug, the number of cells in metaphase increased steadily, while the number in prophase remained constant and the cells in the late phases of mitosis disappeared from the picture. Thus, by a combination of these methods—simple mitosis counts, counts after administration of

From the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital.

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1. (*a*) Buschke, W.; Friedenwald, J. S., and Fleischmann, W.: Studies on the Mitotic Activity of the Corneal Epithelium: Methods; the Effects of Colchicine, Ether, Cocaine, and Ephedrin, Bull. Johns Hopkins Hosp. **73**:143, 1943. (*b*) Friedenwald, J. S., and Buschke, W.: The Influence of Some Experimental Variables on the Epithelial Movements in the Healing of Corneal Wounds, J. Cell. & Comp. Physiol. **23**:95, 1944; (*c*) The Effects of Excitement, of Epinephrine, and of Sympathectomy on the Mitotic Activity of the Corneal Epithelium in Rats, Am. J. Physiol. **141**:689 (July) 1944.

colchicine and phase counts—the course of mitotic activity in the corneal epithelium under the influence of various experimental variables could be studied. By a combination of these three methods it was found that the duration of mitosis in the normal cornea was about seventy minutes,[1a] and the intermitotic interval for the basal cells, approximately one week. Under suitable conditions the mitotic rate could be maintained almost at the normal level in the enucleated eye kept in a moist chamber in the incubator.

TABLE 1.—*Number of Mitoses and Mitotic Rate Under Influence of Neurohormone-Like Substances and Related Drugs* *

Drug	Concentration of Drug, %	Decrease
Pilocarpine hydrochloride	1	—
Physostigmine salicylate	0.25	—
Carbaminoylcholine chloride	5	—
Atropine sulfate	1	—
Histamine phosphate	0.25	—
Epinephrine acetate †	0.01	+
Ephedrine hydrochloride ‡	5	+

* The drugs were applied locally.
† The action of epinephrine was previously reported on.[1c]
‡ The action of ephedrine was previously reported on.[1a]

Neurohormone-Like Substances and Related Drugs.—Histamine was found to be without effect on the mitotic activity. Acetylcholine was likewise ineffective, as were drugs which influence the cholinergic mechanism—physostigmine, carbaminoylcholine chloride and atropine (table 1). Epinephrine, on the other hand, produced a notable inhibition of the entrance of cells into mitosis without disturbing the development of the mitosis once it had begun. By intramuscular injection of epinephrine in peanut oil, mitosis in the cornea can be suppressed for many hours.[1c] Inhibition of mitosis can also be demonstrated when epinephrine is applied to the enucleated eye kept in a moist chamber in an incubator. Ephedrine has an effect similar to that of epinephrine.[2] Ergotamine bitartrate, which inhibits many adrenergic responses, diminishes the effect of epinephrine on the rate of mitosis in the cornea but after several hours ergotamine itself produces some inhibition of mitotic activity.[1e]

Section of the cervical portion of the sympathetic chain or removal of the superior cervical sympathetic ganglion has no influence on the number of mitoses, but use of colchicine to determine the mitotic rate after removal of the superior cervical sympathetic ganglion reveals a pronounced effect, which comes on about twenty hours after removal of the ganglion.[1c] At that time the rate at which cells enter mitosis drops sharply to less than 50 per cent of the normal; at the same time, the rate at which cells pass through the mitotic cycle is similarly decreased. Thus, the number of cells observed in mitosis after ganglionectomy is normal in simple counts but is greatly reduced after administration of colchicine.

Local and General Anesthetics.—Cocaine produces notable inhibition of the initiation of mitosis, similar to that of epinephrine.[1a] Ether has a similar effect, which outlasts the anesthesia for an hour or more.[1a] The effect of ether is to be attributed in part to an outpouring of epinephrine during the stage of excitement of the anesthesia and in part, possibly, to direct action of the ether vapor on the corneal tissue. Barbiturates produced an effect similar to that of sympathetic ganglionectomy, i. e., slowing both of initiation and of progress through mitosis (table 2).

Trauma.—Mechanical damage of less than 0.1 per cent of the epithelial cells of the cornea causes inhibition of mitosis in the remaining, apparently uninjured, cells for several hours.[1b] As will be shown later, the healing of epithelial defects by the movement of cells into the denuded area proceeds actively during this period of inhibition of mitosis. The mechanism of this effect is being studied. It cannot be attributed to a neural reflex, since the inhibition can be demonstrated just as well in the enucleated eye and does not occur when small areas of the corneal epithelium are destroyed by heat. This traumatic inhibition of mitosis complicates the technical problem of studies on the mitotic activity in the cornea of the enucleated eye. However, if care is taken not to injure the cornea during enucleation, the rate of mitosis in the corneal epithelium can be maintained at a nearly normal level.

TABLE 2.—*Mitotic Rate in the Corneal Epithelium of the Rat Under the Influence of Various Anesthetics*

Anesthetic	Dose per Kg. Body Weight	Decrease in Rate
Systemic administration		
Morphine sulfate	30 mg.	+
Barbital sodium	800 mg.	+
Ethyl carbamate	1 Gm.	—
Chloral hydrate	300 mg.	—
Local administration		
Cocaine hydrochloride *	5% ointment	+

* Previously reported on.[1a]

Physical Agents.—Ultraviolet light caused a pronounced inhibition of the initiation of mitosis

2. Buschke, Friedenwald and Fleischmann,[1a] Friedenwald and Buschke.[1c]

(table 3). The inhibition came on after a latent period, which decreased with an increase in the dose of radiation. Exposure to ultraviolet light so slight as to produce no visible clinical symptoms caused severe inhibition of mitosis.

Radiation with beta rays of radium also inhibited the onset of mitosis.[3]

Decrease in temperature to 30 C. did not make it impossible for cells already in mitosis to complete their division. At a temperature of 20 to 24 C. cells in the early phases of mitosis were able to reach metaphase and were "frozen" there, and cells in the late phases of mitosis could still complete their division. At a temperature of 12 C. the whole mitotic cycle was greatly inhibited.

Vitamin A Deficiency.—Deficiency in vitaman A decreased the rate of mitosis and, to a somewhat lesser degree, the progress through the mitotic cycle. The changes were noted at a stage of deficiency at which body growth was arrested, but before severe corneal manifestations had appeared. The effect of vitamin A deficiency resembled that produced by removal of the superior cervical sympathetic ganglion or by barbiturates.

TABLE 3.—*Effect of Ultraviolet Irradiation on Mitosis Counts in Corneal Epithelium of the Rat* *

Length of Exposure	Maximum Inhibition, %	Time of Maximum Inhibition After Irradiation, Hr.
10 sec.	None	
20 sec.	57	> 5
30 sec.	61	> 6
60 sec.	100	24
2½-3 min.†	100	18
10 min.†	100	6

* Irradiation with a small mercury vapor lamp at a distance of 5 mm.

† These doses produce clinically visible damage.

Summary.—A large number of agents have been found which inhibit mitotic activity at various points in the mitotic cycle. So far, the initiation of mitosis and the escape from metaphase appear to be much the most sensitive parts in the cycle. Up to the present we have encountered no agent which produces an increase in the rate of mitosis, though with many substances there is an overshooting of the normal rate of mitosis for a brief period after recovery from inhibition. In no experiment so far carried out has the net excess of mitoses during this phase of recovery exceeded the deficit accumulated during the preceding period of inhibition. The existence of the phase of recovery suggests that there is a premitotic state of the cells. Certain agents apparently inhibit the transition from the premitotic to the actual mitotic state but do not prevent cells from accumulating in the premitotic state. When the inhibition due to such an agent is removed, the accumulated cells in the premitotic condition enter mitosis, and hence this causes an excess of mitoses during recovery.

3. These experiments were carried out in collaboration with Dr. W. F. Hughes Jr. and Dr. Charles E. Iliff Jr., Baltimore.

WOUND HEALING

Method of Assay.—In order to separate the primary phenomenon of wound healing from the inflammatory reaction and secondary infection which complicate the healing of large wounds, we chose for study minute epithelial defects produced by needle pricks of the corneal surface. The method of study has been described elsewhere.[1b] The defects produced were fairly regular and measured about 30 microns in diameter. Specimens fixed immediately after the injury showed that the adjacent cells were flattened in a direction tangential to the hole. One hour later there was no visible change. Two hours after the injury the basal marginal cells had changed their orientation and lay with their long axes radial to the hole. Three hours after the injury the majority of the holes were covered. Thirty or more holes were made in each cornea, and the proportion which showed reorientation of cells at the end of two hours or closure in three hours could be used as a numerical index of the rate of healing. After the initial period of lag, of one hour, the rate of cell movement in closing these small holes was 0.25 microns per minute, a rate which was of the same order of magnitude as the rate of closure of larger defects in the same species. The wound-healing phenomenon proceeded as well in enucleated eyes kept in a moist chamber or in aerated solutions in the incubator as it does in vivo.

Pharmacologic Agents.—Wound healing in the corneal epithelium occurs at a p_H of from 4.5 to 9.5. The process was much less sensitive to pharmacologic interference than was mitosis. Local anesthetics, such as cocaine and tetracaine, inhibited the process, but of the general anesthetics administered systemically, only morphine had a measurable effect. Histamine and acetylcholine and the cholinergic drugs were without effect. Epinephrine and ephedrine were inhibitory, but only when administered in a dose ten times that effective on mitosis. Ephedrine was inhibitory on systemic administration in vivo but was ineffective when administered directly to the enucleated eye in vitro (table 4).

Physical Agents.—Ultraviolet radiation did not inhibit wound healing except in doses producing sloughing of the epithelium, and even in these amounts healing took place up to the time of sloughing and promptly began again from the margin of the slough. Cooling to 30 C. slowed the rate of healing to about one-half. Cooling to 21 C. slowed the rate about tenfold, but some closure of the wound still took place.

TABLE 4.—*Effect of Local Anesthetics, Neurohormone-Like Substances and Related Drugs on Movements of Epithelial Cells in Vitro*

Drug	Concentration, %	Inhibition of Movements
Pilocarpine hydrochloride	0.5	—
Physostigmine salicylate	0.5	—
Carbaminoylcholine chloride	0.1	—
Atropine sulfate	0.5	—
Epinephrine hydrochloride	0.001	±
Ephedrine sulfate	0.5	—
Histamine dihydrochloride	0.25	—
Cocaine hydrochloride	0.25	+
Butacaine sulfate	0.25	+
Phenacaine hydrochloride	<0.16	+
Chlorobutanol	<0.16	+
Tetracaine hydrochloride	0.125	+

Metabolic Inhibitors.—Anoxia, sodium cyanide and sodium azide inhibited the healing process. The inhibition resulting from anoxia was completely reversible if oxygen was readmitted after a period of deficiency as long as three hours. The somewhat less regularly reproducible inhibition due to cyanide was also reversed if the tissue was transferred to a cyanide-free bathing fluid. It was not reversed by the addition of small amounts of methylthionine chloride in the presence of cyanide, amounts of methylthionine chloride which have been shown to reestablish respiration of cells poisoned by cyanide.[4] Sodium iodoacetate also inhibited the healing process, and this inhibition was not reversed by the addition of glutathione after removal of the excess iodoacetate. Inhibition also was not reversed by the addition of pyruvate, succinate or fumarate. Inhibition by iodoacetate is, therefore, not attributable to lack either of glutathione or of the carbohydrate breakdown products of glycolysis. Further support for the second conclusion is seen in the relative insensitivity of the healing mechanism to fluoride poisoning. The results of experiments with these and with other metabolic poisons are shown in table 5.

Summary.—The healing of small epithelial defects of the cornea proceeds to the point of closure of the defect in the absence of any multiplication of cells. Experiments carried on by Arey and Covode [5] with larger defects indicated that even in these wounds the inhibition of mitosis outlasts the time required for closure of the wound. The cells covering a defect are larger and flatter than normal, and at first form a layer of only one cell. Thus, coverage of an epithelial defect can be accomplished with far fewer cells than were initially present. In the phase of mitotic activity following the traumatic inhibition, the deficit of mitoses accumulated during the inhibition is only partly made good. Thus, recovery of the normal number of epithelial cells must be accomplished by a reduction in the rate of desquamation following closure of the wound. The period of lag of one hour following injury before the onset of cellular movements is of special interest, since it is apparently during this period that the stimulus for cell movement becomes established.

It should be pointed out that the experiments here reported on concern the healing of small wounds. It is quite possible that in the healing of larger epithelial defects different, or more complicated, processes are involved. We chose to study first the small lesions described here because they were more accessible to experimental study and because we wished to eliminate from the experiments a complicating feature of larger injuries, namely, inflammatory reactions.

TABLE 5.—*Inhibition of Movement of Epithelial Cells by Enzyme Poisons and by Anoxia*

	Concentration	Inhibition
Anoxia	.....	+
Sodium cyanide	M/1,000	+
Sodium azide	M/2,000	+
Sodium iodoacetate	M/1,000	+
Sodium fluoride	M/50	—
Sodium malonate	M/100	—
Sodium dinitrophenol	M/1,000	+
Sodium arsenite	M/1,000	+
Sodium arsenate	M/500	+
d l-glyceraldehyde	M/100	+
Thiourea	M/75	—
Thiosinamine (allylthiourea)	M/120	—
Sodium diethyldithiocarbamate	M/160	—
Oxyquinoline	M/150	+

Wilmer Ophthalmological Institute.

4. Barron, E. S. G.: Studies on Blood Cell Metabolism: III. The Effect of Methylene Blue on the Oxygen Consumption of the Eggs of the Sea Urchin and Starfish; the Mechanism of the Action of Methylene Blue on Living Cells, J. Biol. Chem. **81**:445, 1929.

5. Arey, L. B., and Covode, W. M.: The Method of Repair in Epithelial Wounds of the Cornea, Anat. Rec. **86**:75, 1943.

CORDITE AS AN INTRAOCULAR FOREIGN BODY

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The presence of cordite alone as an intraocular foreign body is apparently unusual. Only one reference to such a condition was found in the available literature. Probably cordite has been introduced into the eyes in many wounds due to explosions, but the entrance of the powder has been overshadowed by extensive damage or by the presence of other foreign material.

Two cases are presented in which cordite was introduced into the eye. Cordite [1] is a smokeless powder composed of glyceryl trinitrate, guncotton and petrolatum. Glyceryl trinitrate is somewhat soluble in water but is not locally irritant to tissues. Guncotton [2] and petrolatum are relatively inert. Goulden and Whiting [3] stated:

> Particles of quartz, cordite, or an eyelash (unless the follicle be included) may remain in the eye indefinitely without causing trouble, and unless visible in the anterior chamber and easily reached are best left alone in view of the difficulty and danger involved in their removal.

This statement confirms my own experience. No other reference to the intraocular occurrence of cordite was found in the literature, although Cunningham [4] described a case in which a particle of the substance was embedded in the cornea, from which it was easily extracted.

REPORT OF CASES

CASE 1.—The patient was flying in target practice at about 9 o'clock, May 17, 1943, when a machine gun jammed, and the cartridge backfired. The left side of his face and his left eye were spattered by the exploding powder. He was taken to the nearest station hospital, where he received an injection of morphine, and was admitted to the regional station hospital three and a half hours later. His face, particularly the upper left side, was spattered with black, partly burned, cordite, which was driven rather deeply below the surface of the skin. Vision in the right eye was 20/20 and the eye was normal. Vision in the left eye was limited to light perception, without accurate projection. There was a perforating, semicircular wound of the cornea, about 2.5 mm. in diameter, at about 3:30 o'clock on the limbus; the wound was closed at the time of the examination. Most of the epithelium of the cornea was rough and slightly opaque. The anterior chamber was full and seemed to be grossly clear. The temporal side of the iris, behind the corneal perforation, appeared to be absent, but visualization was not good enough for one to determine whether this was the result of retroplacement or of tearing away of the iris. The anterior capsule of the lens was irregular. The cortex was opaque, and no fundus reflex was obtained. A prophylactic dose of Clostridium tetani, Bacillus welchi and Vibrio septicus was given. Roentgenographic examination showed no evidence of any opaque foreign body in the left eye or anywhere in the head.

Instillation of atropine was ordered for the left eye, and applications of wet compresses saturated with boric acid, alternating with instillation of sulfathiazole ointment, were employed every two hours for the face. Sulfadiazine was given by mouth. In two days the major portion of the powder had come out of the skin of the face, and the cornea of the left eye had epithelized. It could now be seen that there was a coloboma of the iris at 4:30 o'clock, but the absent iris tissue could not be found. There was slight ectasia of the cornea at the site of the perforation; this disappeared after application of a pressure dressing for two weeks. Intravenous injections of typhoid bacilli, as foreign protein therapy, and administration of sulfadiazine were used alternately from the time of the patient's admission through September because of the persistence of moderate ciliary injection, corneal precipitates and aqueous floaters. On July 14 a linear extraction was performed to remove the lens material, which was not absorbing rapidly and some of which remained in the lower part of the anterior chamber. On July 20 the pupillary opening had cleared sufficiently for one to see considerable clotted blood in the anterior part of the vitreous, but the fundus could not be visualized. By the middle of September, however, the blood had contracted to a large white, nebulous mass in the anterior portion of the vitreous, behind the coloboma of the iris. The fundus appeared grossly normal. The patient was discharged on October 27, at which time the nebulous mass in the anterior part of the vitreous had contracted still more. The fundus was normal, and there was no inflammation. Vision was 20/15 in the right eye; with a correction of +11.50 D. sph.⌒ — 1.50 D. cyl., axis 135 it was 20/20 in the left eye. The patient was last seen on Jan. 18, 1944, at which time both eyes were quiet. Vision was 20/15 in the right eye and was correctible to 20/20/6 in the left eye. The tension was 17 mm. in the right eye and 19 mm. (Schiøtz) in the left eye.

CASE 2.—This flier was in the same accident as the patient in case 1, with approximately the same injuries

1. Norris, J. F., and Young, R. C.: Textbook of Inorganic Chemistry, ed. 2, New York, McGraw-Hill Book Company, Inc., 1938, p. 342.

2. Jacobs, M. B.: Analytical Chemistry of Industrial Poisons, Hazards and Solvents, New York, Interscience Publishers, Inc., 1941, p. 522.

3. Goulden, C., and Whiting, M. H., in Bailey, H.: Surgery of Modern Warfare, ed. 2, Baltimore, Williams & Wilkins Company, 1942, vol. 2, p. 855.

4. Cunningham, J. F.: Notes of Some War Wounds of the Eye and Orbit, Ophthalmoscope **14**:412, 1916.

except that they were more severe. He was admitted to the hospital at the same time. The skin of his entire face contained more partly burned cordite than did that of the first patient. His nose was almost black. There were multiple lacerations and through and through perforations of the right cornea, one of which almost completely divided the cornea vertically through its center. However, the perforations were all closed, and no aqueous was leaking. The lens was badly macerated, and its fragments were distributed through the anterior chamber. An air bubble 2 mm. in diameter and other, smaller ones were present in the upper part of the anterior chamber. The pupil was dilated, and there were many small perforations of the iris. There was doubtful perception of light. Multiple minor lacerations of the cornea of the left eye and numerous intracorneal blackened, nonmetallic foreign bodies were noted. A large white, opaque intracorneal foreign body was present near the center at 4 o'clock. The anterior chamber was clear, and the disk and fundus appeared grossly normal. Vision was limited to perception of hand movements at 1 foot (30 cm.). Roentgenographic examination showed no foreign bodies in the eyes or head.

Initial treatment was identical with that in the first case. Application of wet compresses of boric acid for several days was required to remove the cordite from the skin, for the particles were more numerous and were driven in deeper. The right cornea became somewhat ectatic in the center but resumed its normal curvature after application of a pressure dressing for two weeks. The intracorneal foreign bodies of the left eye came out spontaneously, and after a week this eye required no treatment. The right eye, although more severely wounded than the injured eye in the first case, had much less inflammatory reaction, and by the end of July the process seemed practically quiescent. However, considerable pupillary membrane remained, so that the interior of the eye could not be seen. On July 31 a crucial discission was done with a Wheeler knife, a good pupillary opening resulting. The patient was discharged to duty on August 9. At that time there was a large, slightly nebulous, deep opacification in the center of the right cornea. The iris was frayed and moth-eaten by many lacerations and perforations. The vitreous was clear; the fundus was normal, and no evidence of any foreign body could be seen. Vision was 20/40 with a correction of + 12.00 D. sph. ⌒ — 2.00 D. cyl., axis 30. The diminution of vision was undoubtedly due to the nebulous central scar in the cornea. Vision in the left eye was 20/20. This eye was normal except for multiple superficial scars in the cornea. The patient was seen subsequently in December 1943, when no change in the appearance of the right eye or in visual acuity was noted.

SUMMARY

The mass in the vitreous in the first case may have contained cordite with a surrounding blood clot. In the second case the cordite must have been entirely absorbed and have disappeared from the eye within six weeks after its introduction, without leaving any residue, producing any toxic effects or introducing any grossly infectious material into the eye. From the uneventful recovery and satisfactory visual results in these 2 cases, it seems that cordite as an intraocular foreign body is in itself relatively innocuous, and conservative treatment should be employed.

COMPLICATED CATARACT ASSOCIATED WITH SPONTANEOUS DETACHMENT OF THE RETINA

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In three recent papers I discussed and illustrated the pathologic changes in the lens in cases of perforating ulcer of the cornea,[1] leukoma adherens [2] and spontaneous iritis [3] respectively. In each condition the primary lesion held to be the cause of the cataract was located in the anterior part of the globe. In the condition discussed in this paper, the fourth in sequence, the primary lesion was located in the posterior half of the eye. The purpose of these studies has been to ascertain the changes which may occur in a lens as a result of various pathologic conditions in the globe.

Clinically, there is considerable difference in the appearance of cataracts. The cataract that is associated with a retinal detachment often has a peculiar yellowish white hue, which is all the more noticeable because the pupil in a case of detachment, as a rule, is not small and is seldom covered by a membrane.

MATERIAL

The material consisted of microscopic preparations of lenses from 21 globes, for 12 of which a history was obtained. Although it was known that some of the detachments had existed from two months to twenty-five years, there was no mention of a similar condition in the fellow eye. In a paper on the pathologic picture of retinal detachment,[4] I reported on the examination of 41 globes, for 28 of which a history was obtained. Here, also, there was no mention of bilateral involvement, although it was known that some of the detachments had existed from five months to twenty-five years. These figures are informative as to how brief or how long a period a globe may tolerate a detached retina before iritis and secondary glaucoma necessitate its removal. It was striking that of the 21 globes, 11 were associated with a history or anatomic signs of myopia. Certainly, not one-half the detachments seen clinically are in myopic globes. It is pathologic experience that most myopic globes show inflammatory foci in various parts. Probably this explains why complications are more likely to develop with retinal detachment in myopic globes than in other globes—hence the predominance of myopic globes in pathologic material. The ages of the patients in the present series, when given, ranged from 7 to 83 years, and those in the former series, when given, from 1 to 80 years.

In both series only cases of spontaneous detachment were chosen, those being excluded in which the condition was caused by tumor, exudative retinitis (Coats's disease), angiomatosis of the retina (von Hippel's disease) and retinitis interna and externa, which fall into the category of secondary detachments. Cases in which operation was performed to replace a spontaneous detachment were excluded because there would have arisen the difficult question as to how much of the damage to the lens and other parts of the globe should be attributed to the original detachment and how much to the subsequent operation.

A majority of the 21 globes were removed because of development of the well known triad that may follow sooner or later in the wake of the detached retina, namely, iritis, secondary glaucoma and cataract. A globe with an old detachment or one with a potential detachment stands ever so slight a blow badly. In the present series a myopic globe that had been sensitive for three years met with a slight contusion four months before enucleation, which caused hyphemia and excruciating pain. In another myopic globe a detachment following contusion had existed in a quiescent state for six years. Two weeks before enucleation the eye suffered a second contusion, which caused a violent inflammatory process. The second case fell into the category of borderline cases, in which it is difficult to decide whether a detachment is really spontaneous or is due to an alleged direct or indirect injury.

PREEXISTING INFLAMMATION

In all probability, in many cases iritis should not be considered a complication of a detached retina but, rather, should be regarded as a sequel of a hidden inflammatory process that antedated the detachment and was, in fact, the original cause of it. It is conceivable that such an inflammatory condition would be aggravated by the detachment of which it had been the cause and would lead soon to iritis and secondary glaucoma. In support of this theory are the cases in which a detachment starts with outspoken iritis, a vitreous full of opacities and hypotension. At times, weeks after a successful operation, showers of dustlike opacities in the vitreous portend a second detachment. Even with malignant melanoma of the choroid it is known that iritis may appear

Read at the Eighteenth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., May 29, 1944.

1. Samuels, B.: Tr. Am. Ophth. Soc. **39**:66, 1941.
2. Samuels, B.: Tr. Am. Ophth. Soc. **40**:292, 1942.
3. Samuels, B.: Tr. Am. Ophth. Soc. **41**:262, 1943.
4. Samuels, B.: Pathologic Picture of Retinal Detachment, Arch. Ophth. **21**:273 (Feb.) 1939.

soon after the retina becomes detached, and before the tumor itself becomes necrotic and toxic.

Occasionally a detachment causes a complicated cataract without any sign of inflammation, either clinical or pathologic, in the anterior part of the globe. A case of this kind was studied in the present material (fig. 1). The iris and the ciliary body were normal, and so was the choroid except for a small inflammatory patch near the ora serrata. The retina was completely detached and exceedingly gliosed and degenerated. A thin, but widespread, cataract was present in the anterior capsule. A broad row of vesicular cells lined the posterior capsule. Later it will be stated how often the latter change occurs with the cataract of detached retina.

CAUSES OTHER THAN THE DETACHMENT THAT WERE BELIEVED TO HAVE CONTRIBUTED TO DEVELOPMENT OF THE CATARACT

Iritis.—The cause of the inflammation of the iris associated with retinal detachment has never been clearly explained. However, that the iritis is produced by toxins in the stagnant subretinal fluid seems to be proved by the procedure of puncturing the sclera and allowing the fluid to escape, as advocated by Meller, of Vienna, after which, more often than not, the iritis quiets down. In this study it frequently was not easy to decide whether a cataract had been caused by the detachment alone or by the iritis alone or by a combination of the two, either condition being able independently to produce a cataract.

In the paper on the cataract of spontaneous iritis it was stated that only after repeated attacks of iritis is the lens damaged. In the iritis associated with detachment of the retina the inflammation is usually severe from the start and almost never has a period of complete abatement. There was no doubt that iritis was a factor, if not the chief one, in the causation of the cataracts in 5 globes with iris bombé, in 3 globes with a complete posterior synechia and in 2 globes with a pupillary membrane (fig. 2). These observations demonstrated how severe this type of iritis can be.

Altered Metabolism.—A second factor considered to have exerted an unfavorable influence on the lens was interference with the outflow of the intraocular fluid into the papilla. In a case of detachment, especially when the papilla is covered by the detached retina, the flow of the intraocular lymph toward the brain must be impeded, so that the fluid stagnates and undergoes chemical change. Then, too, a disturbance of the general metabolism of the body may set up inflammation in a diseased globe, whereas it might have no effect on a sound eye.

Glaucoma.—A third factor, one known to have a deleterious effect on a lens, was secondary glaucoma. A cataractous lens is nearly always a complication of glaucoma, of whatever type. The tension in 13 of the globes, according to the history or to the results of anatomic examination, had been high. In 1 globe a wrinkled choroid was evidence of hypotony at one period, whereas peripheral anterior synechia implied glaucoma at the time of enucleation.

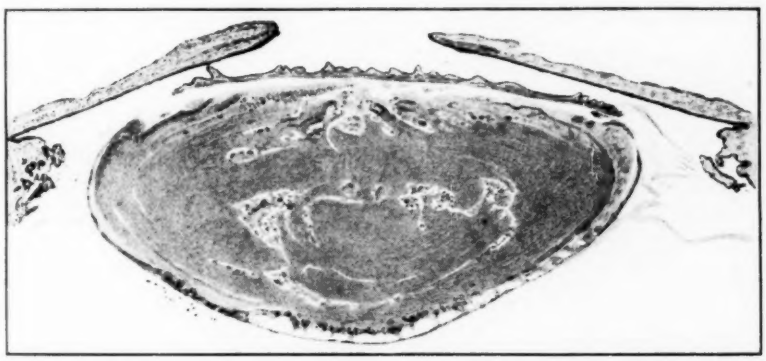

Fig. 1.—The entire lens is cataractous. An artefact separates the anterior capsule from the nucleus. The cataract has thrown the capsule into sharp folds. A row of vesicular cells lines the posterior capsule.

STATE OF THE INTRAOCULAR CONTENTS

Retina.—The retina in most instances was completely detached and gliosed. In 1 globe the part of the retina that remained with the choroid was permeated with blood, as is seen occasionally after a surgical reattachment. No matter whether the detachment had existed for a long or for a short period, the retina was always severely damaged. It is possible that the first effects of the stagnant fluid were exerted on the overlying retina, which even before the separation was probably far from normal in many instances. Actual necrosis, such as occurs in septic endophthalmitis, was never encountered.

No doubt the disintegrating structure of the retina added its quota to the irritating substances. Neither was the retina as compactly folded by membranes as in cases of endophthalmitis. For this reason, the retina remained at some distance from the lens, only occasionally touching it.

Because of the unsightly appearance of the pupil, one is often pressed to operate for cosmetic purposes. It is well to remember that, owing to the space which usually intervenes between the folded retina and the lens, a cataract in a case of spontaneous detachment should lend itself with safety to removal. However, the extracapsular method is preferred because, if the posterior capsule is ruptured or removed, cellular elements that may be harmless in the anterior chamber, once they enter the vitreous cavity, are not readily absorbed and may be very irritating.

Subretinal Fluid.—In most instances the subretinal fluid was clear and less albuminous than that in cases of recent detachment. It was not the original fluid from the liquefied vitreous that escaped through a hole or a tear in the retina. The fluid examined was propably a transudate derived from the impaired circulation in the retina. Several times a large quantity of blood was encountered in the subretinal space. Clotted blood in the chambers of the globe, as it becomes necrotic, is especially irritating. It is well to remember that when blood occurs in large amount under the retina, it may cast a shadow by transillumination and simulate a tumor of the choroid.

Choroid.—The choroid was nearly always free of signs of active inflammation, although now and then a small lymphocytic focus appeared, as was to be expected in globes with an old inflammatory process. There was no evidence that the choroid was the source of the subretinal fluid, particularly since the pigment epithelium was never raised, as one would have expected it to be if the transudate had come from the choroid. In 1 globe there were drusen, but these bodies may have been laid down before the retina separated. One globe showed lymphocytic foci on the external surface of the sclera—probably a cause of part of the pain.

Of particular interest in several globes, as evidence of excessive irritation by the confined fluid, was a large *Ringschwiele* in the angle of detachment at the ora serrata. Ossification of the choroid was not noted, doubtless because of the absence of organized membranes on the internal surface of the choroid.

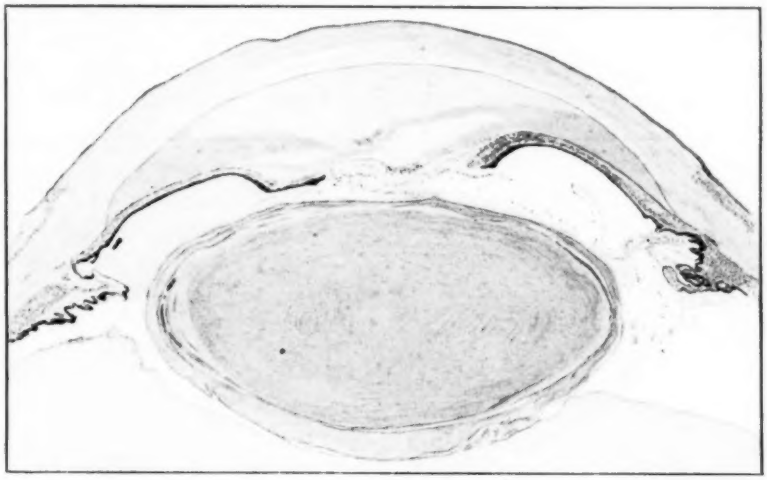

Fig. 2.—After detachment of the retina, inflammation developed, with iris bombé and seclusion and occlusion of the pupil. Blood and albuminous fluid fill the anterior chamber. The cortex of the lens is entirely broken down. The capsule is detached at some points. Calcification has taken place at one equator. To the right, delicate membranes cross from the ciliary body to the lens.

In the entire series of 21 globes but 1 tear or hole was discovered in the retina. It was realized that in serial sections others might have been discovered. In most of the globes the detachments were old, so that if there had been apertures they would probably long since have been sealed by membranes or have been concealed between the folds. When there is a communication between the vitreous and the subretinal fluid, it might be spoken of as an "open" detachment; and when there is none, it might be called a "closed" detachment, in the sense of open or closed empyema. One might speculate as to whether the toxins in a case of a "closed" detachment are more concentrated and irritating than those in a case of an "open" detachment.

Vitreous.—Specimens from 17 globes permitted an examination of the vitreous between the retinal folds or anterior to them. In 5 cases the vitreous was detached and in 5 others it was traversed by membranes. In 3 cases it contained blood. In 1 case it was entirely clear, and in another it was shrunken to the form of a membrane. In 5 cases the vitreous was detached. A "step" in the retina at the point of a detachment of the vitreous is an anatomic sign of traction. It was noteworthy that in one-third the cases in which an adequate study could be made the vitreous was detached. This observation spoke in favor of the Leber-Gonin-Lindner theory [4] that most retinal detachments are the result of traction by strands of broken-down vitreous or by traction from a detached vitreous as a whole.

Iris.—In 10 globes the iris showed lymphocytic infiltration and small adhesions to the lens. The occurrence of iris bombé and complete posterior synechia has already been noted. Clinically, iris bombé in a globe that is known to have been blind for a long time may well be considered as a sign of retinal detachment. That the iris was often severely irritated and the ciliary body seldom so was explained by the fact that the iris has two surfaces to be bathed in a toxic aqueous, whereas the ciliary body has one; besides, the ciliary body is probably more resistant than the iris.

THE LENS

Localization. — Occasionally the lens was slightly dislocated backward. In 1 case the lens was pulled to one side by a membrane derived from the ciliary body, and in several cases filaments from membranes on the ciliary body stretched across the circumlental space to lose themselves on the equator of the lens. It is these adhesions that may bring about complications in an intracapsular extraction.

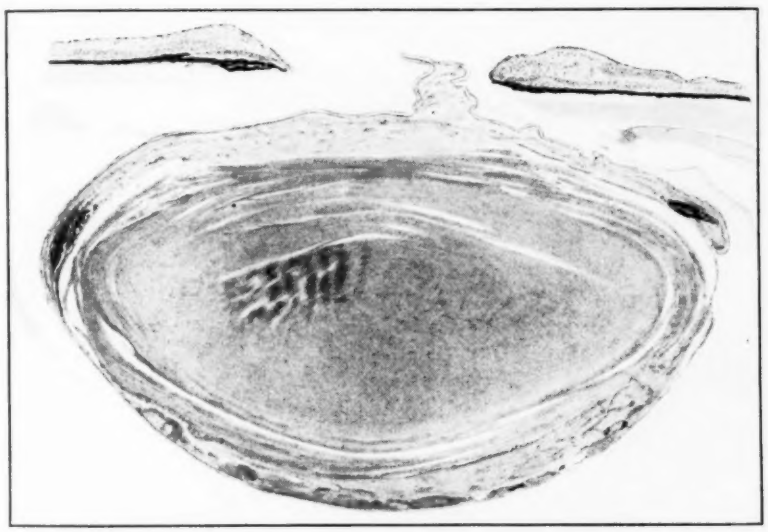

Fig. 3.—An unusually large cataract in the anterior capsule shows an irregular pyramidal process jutting forward in the pupillary area. At its equatorial margin the cataract has undergone calcification. The posterior capsule is lined by vesicular cells.

Ciliary Body.—In 14 globes the ciliary body was either normal or only sparingly infiltrated. In 2 globes the ciliary body was merely atrophic, probably as a result of glaucoma. One globe was interesting in that, in the absence of cyclitis, there was a large pyramidal cataract. However, there were a severe iritis and a greatly degenerated retina to account for it. In 1 globe the tension was said to have been very "low." The detachment had existed one year. Five days before enucleation the eye became inflamed and painful. The hypotony seemed to be explained by the presence of lymphocytic foci in the ciliary body. In 5 globes there was a membrane on the internal surface of the ciliary structure—alway more delicate than that of an ordinary cyclitic membrane.

Anterior Subcapsular Epithelium. — The changes in the epithelium of the anterior capsule were always noticeable. In 4 cases there was a large pyramidal cataract (fig. 3) and in 11 others there was extensive proliferation of the epithelium beneath the anterior capsule. In cases in which there was no adhesion between the iris and the lens, the cataract was believed to have been produced chiefly by irritating substances from the posterior part of the globe.

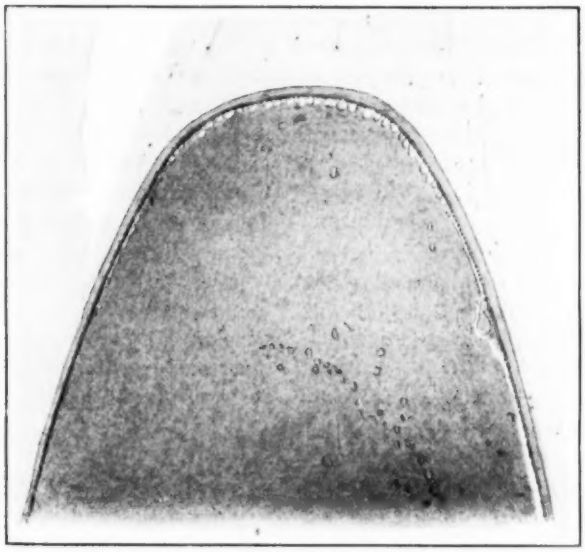

Fig. 4.—The epithelium of the anterior capsule is similar to that of the posterior capsule. The germinal zone has entirely disappeared. A row of lightly stained droplets is evidence of fluidity of the lens.

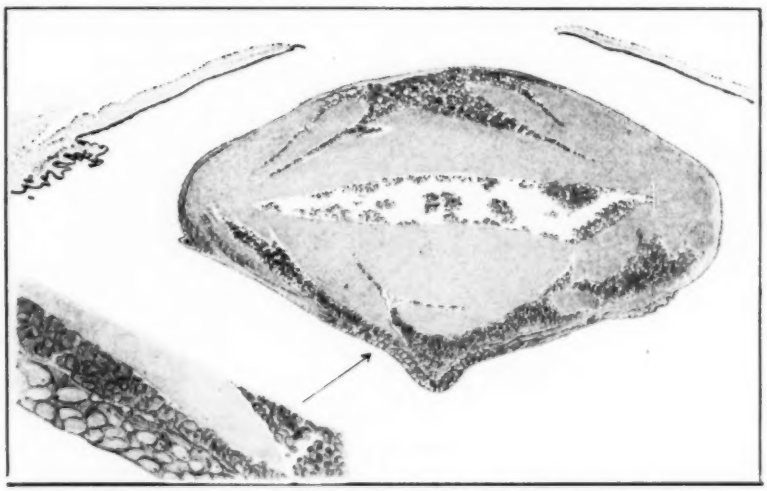

Fig. 5.—A layer of vesicular cells, several cells in thickness, lines the posterior capsule, whereas a single layer of ordinary subcapsular epithelium lines the equator. In the detail, the vesicular cells are separated by a layer of debris from a projection of the nucleus of the lens. To the right are morgagnian globules.

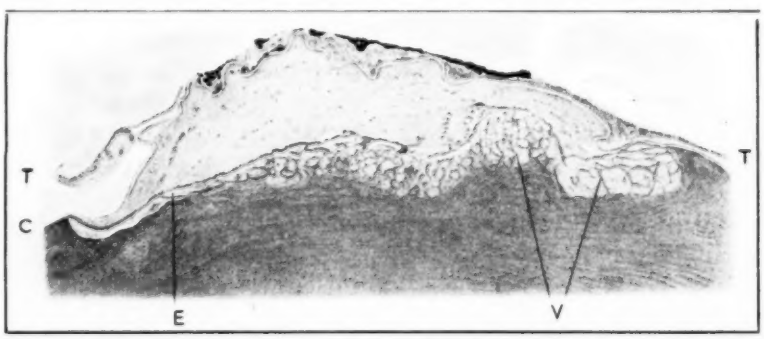

Fig. 6.—The anterior half of a cataractous lens after chronic iritis in a case of detachment of the retina. The lens capsule (*C*) is elevated and thrown into numerous folds by a pyramidal proliferation. The latter is outlined posteriorly by an irregular layer of epithelium (*E*). Within the cataract there is a scattering of epithelial cells. A broad zone of vesicular cells (*V*) separates the cataract from the nucleus of the lens. Vesicular cells as a rule are seen on the posterior capsule. Here, they were present only anteriorly. The lens capsule is covered by homogeneous connective tissue, which, in turn, is covered by adherent pigment epithelium from the iris. On either side a thread (*T*) points toward the ciliary body, forming a dangerous lens-ciliary synechia, which frequently causes operative complications.

Fully one third of the cases fell into a unique category in that a single row of epithelial cells lined the entire inner surface of the capsule (fig. 4).

Germinal Zone.—As a majority of the cataracts were total, the germinal cells had nearly always disappeared or were in great disorder, so that the growth of the lens had ceased. Concurrent with the loss of the lens fiber–producing cells, the cuboid cells of the anterior subcapsule had proliferated equatorially to take their place (fig. 4).

Vesicular Cells.—In practically every lens large vesicular cells, which were germinal cells endeavoring to form lens fibers, were encountered in great numbers. In more than one-half the lenses these cells lay on the posterior capsule (fig. 5 *A*). In several lenses, as an exception, they were misplaced forward. In 1 lens they formed a layer between the anterior capsular cataract and the lens substance (fig. 5 *B*). In 1 lens (fig. 6 *A*) the transition of vesicular cells into epithelial connective tissue could be seen within the cataract itself.

Lens Substance.—The cortical substance as a rule was liquefied, and in several lenses it was calcified. The nucleus was more or less disintegrated, this change usually corresponding to the age of the patient. In but 2 cases was the lens substance entirely liquefied (fig. 4). However dead a lens may appear clinically, it is likely that microscopic study will reveal living cells in it.

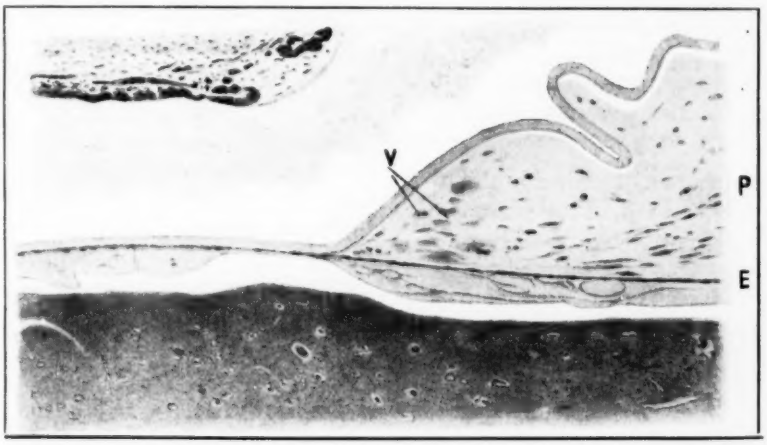

Fig. 7.—A pyramidal cataract (*P*). Most of the cells have become spindle shaped. They have laid down a peculiar, connective tissue–like substance. At *V* a number of small light spots reveal lens material formed by vesicular cells. Capsular epithelium (*E*) bisects the capsular cataract.

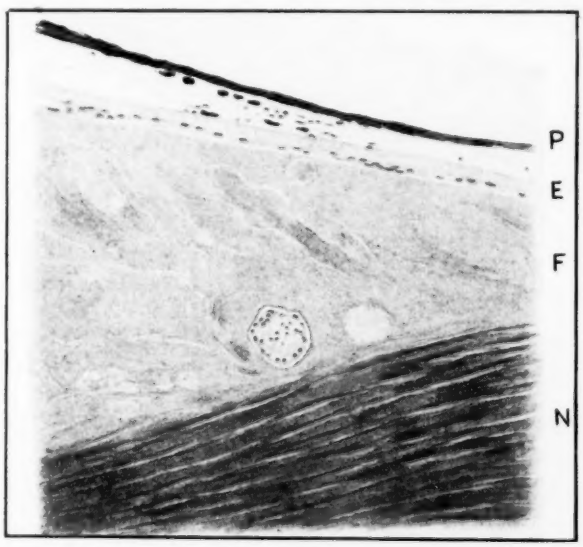

Fig. 8.—An epithelial precipitate in the lens. The capsular epithelium (*E*) is separated from the nucleus (*N*) by the fluid cortex, in which a cellular spherical mass must have floated around in life. A pigment layer (*P*), having fallen away from the iris, rests on the anterior capsule.

Epithelial Sphere.—The globe presenting this lesion was that of a 7 year old boy. In the liquefied cortex was a freely movable cellular sphere (fig. 6 *B*). This was believed to represent a circumscribed proliferation of cells that had broken away from the capsule and, by floating about in a liquid, had become globular. A similar formation is seen as a rarity in the aqueous of the anterior chamber, derived from detached endothelial cells. In the 92 lenses studied in the four series this was the only epithelial sphere encountered.

LENTICULAR CHANGES CHARACTERISTIC OF SPONTANEOUS DETACHMENT OF THE RETINA

Practically every change described in the three previous series was observed in the present one, an indication that the pathologic changes which may occur in this organ are limited in kind. However, when this series was compared with the three previous series as to the extent of the changes, their frequency and their distribution, the following characteristics of cataract associated with spontaneous retinal detachment are apparent:

1. The presence of well defined vesicular cells in the posterior quadrant of the lens. These cells were observed to occur in far greater abundance and frequency than was seen in the other series (fig. 5 *A*).

2. The lining of the entire capsule by a single layer of epithelial cells. This happened with far greater frequency than was noted before.

CONCLUSION

The presence of epithelial cells in the posterior quadrant of the lens, where normally there are no cells, implied that they had proliferated in that direction in response either to a chemical agent or to an impulse inherent in them to grow backward.

57 West Fifty-Seventh Street.

Correspondence

OCULAR TUBERCULOSIS

To the Editor:—In the June 1944 issue of the ARCHIVES there appears an article entitled "Ocular Tuberculosis: Its Relation to General Tuberculosis," by Dr. Benjamin L. Gordon. The first section of this paper is a historical review of tuberculosis, with particular reference to ocular tuberculosis. In view of the generally high scientific level of the papers appearing in the ARCHIVES, it is shocking to find the historical section of this paper replete with errors. As the journal has a wide circulation, I believe that such misstatements may become widespread. I am therefore taking the liberty to point out these errors in the hope that the correct information will be presented.

On page 541 Dr. Gordon states: "Hippocrates had no other diagnostic procedures at his disposal than simple inspection and palpation. He had no stethoscope and no experience in percussion and auscultation." This statement with regard to auscultation is erroneous. There is little doubt that direct, or immediate, auscultation was employed from the earliest times. Auscultation is mentioned in the Papyrus Ebers and in the "Ayur-Veda" and was known to Hippocrates. For a brief and easily accessible discussion of this matter one may refer to Webb's masterly little book "Tuberculosis" (XVI., Clio Medica: A Series of Primers on the History of Medicine, edited by E. B. Krumbhaar, New York, Paul B. Hoeber, Inc., 1936, pp. 123-124).

On page 542 Gordon states that Thucydides "expressed a definite belief in the infectious character of plague." One may be permitted to doubt whether the epidemic disease that prevailed in Athens was bubonic plague—despite all the controversy, this point is still unclear—and, second, whether Thucydides knew that it was what is now known as bubonic plague. In view of the fact that the Greeks did not generally distinguish disease entities, it is hardly likely that this was done by Thucydides.

On page 543 Antoine Maître-Jan is described as a physician, which is erroneous. He was a surgeon, a distinction which was a matter of some significance in the eighteenth century.

On page 547 occur two misstatements that are inexcusable. In a short biographic sketch of Robert Koch, it is pointed out that he went to the University of Göttingen, where Henle was professor of anatomy. "At that period," says Dr. Gordon, "Henle published his famous essay, entitled 'Miasmata and Contagia.'" Now Koch did not enter Göttingen until 1862, while Henle published his essay in 1840, in a book entitled "Pathologische Untersuchungen." At this time he received an appointment as professor at the University of Zurich. Henle did not go to Göttingen until 1852, ten years before Koch's matriculation there, and his essay was published twenty-two years before Koch entered the school. (For a documented account see Bruno Heymann: Robert Koch, Part 1: 1843-1882. Grosse Männer, vol. XII. Leipzig, Akademische Verlagsgesellschaft, 1932).

On the same page, Dr. Gordon states that after graduation Koch settled in the "town of Wollstein, in the province of Pausen, Czechoslovakia." This is wrong. Koch became the district physician (*Kreisphysikus*) in the district of Bomst. He lived in Wollstein, a town in the province of Posen, which was then part of the German Empire and at the end of World War I became part of Poland. After 1939 this district was again incorporated into Germany and received the name of Warthegau, or Reichsgau Wartheland. It was never at any time in Czechoslovakia. One would like to know where Dr. Gordon got his information.

I should like also to call attention to footnote 18, on page 545, in which the author makes the curious statement that Helmholtz inherited his modesty, refined life and simple taste from his mother. It seems odd to find such a statement, which harks back to the days when nothing was known about the mechanism of heredity, in an up-to-date scientific journal like the ARCHIVES. It would be enlightening to know the mechanism by which modesty or a refined life or a simple taste is inherited.

In conclusion, may I suggest that the history of medicine ought to be handled as accurately and conscientiously as any clinical subject? It is indeed high time that physicians who would not dream of employing the theory of the humors in the discussion of clinical materials desist from the use of analogous approaches in dealing with the history of their subject. May I also suggest that a journal, such as the ARCHIVES, which presents historical articles ought to have a consulting editor who is a medical historian and is capable of dealing critically with these materials?

CAPTAIN GEORGE ROSEN, Medical Corps,
Army of the United States.

To the Editor:—I am amazed to read the statement of Dr. Rosen that my paper is replete with errors which may reflect on the scientific level of the ARCHIVES. As a professional medical historian, it would be well for Dr. Rosen to investigate further the historical facts before making such a charge.

In the first place, Dr. Rosen finds fault with my statement: "Hippocrates had no other diagnostic procedures at his disposal than simple inspection and palpation. He had no stethoscope and no experience in percussion and auscultation." In this sentence "stethoscope" carries the connotation of indirect auscultation. I am sure that Dr. Rosen will agree that Hippocrates did not use a stethoscope, even granted that direct, or immediate, auscultation may have been employed from the earliest times. Hippocratic "succussion," referred to in his works, was a method of shaking the body in order to observe the splashing sounds which may be heard when fluid accumulates in the pleural or the abdominal cavity.

I presume that in his reference to the "Papyrus Ebers" Dr. Rosen has in mind the vague phrase "Here the ears hear beneath," which could easily allude to direct auscultation of the heart or intestine, and not to auscultation of the lungs, which of course is the only concern of my article.

The credit for the discovery of indirect auscultation as a diagnostic measure belongs to Laënnec. To cite Osler, "The discovery of auscultation by Laënnec and the publication of his work, 'De l'auscultation médiate,' marked an era in the study of medicine" (Evolution of Modern Medicine, New Haven, Yale University Press, 1921, p. 203).

Dr. Rosen takes exception to my statement that the historian Thucydides expressed a definite belief in the infectious character of the plague. This assertion is based on Thucydides' own statement. In describing the plague of Athens, he states: "Nay, they [physicians] themselves died most of all, inasmuch as they most visited the sick."[1] Dr. Rosen questions the statement of Thucydides because he is of the opinion that the Greeks did not generally distinguish disease entities. This view of Dr. Rosen's is open to debate. He certainly will not deny that in the time of Hippocrates (460-370 B.C.) diseases were distinguished as separate entities. Thucydides (460-400 B.C.) was a contemporary of Hippocrates and certainly was aware of disease entities.

The most unusual criticism by Dr. Rosen is the complaint that I classed Antoine Maitre-Jan as a physician rather than as a surgeon. Maitre-Jan is well known as "the father of French ophthalmology." His principal work, "Traité des maladies d'oeil, et des remèdes propres pour leur guérison" (Troyes, 1707; Paris, 1722 and 1741), consisting of 570 large pages, deals mainly with the nature of vision, experiments relating to the camera obscura, the laws of optics and the treatment of diseases of the eye—subjects not especially surgical. From an ophthalmologic point of view Maître-Jan was a physician.

I regret that I did not give the date on which Henle published his essay "Miasmata and Contagia." The term "period" was not intended to convey the impression that it was written when Koch was a student in Göttingen. Koch, after serving through the Franco-Prussian War and after a brief residence in Rachowitz, became district physician at Wollstein, where he remained for ten years.

In footnote 18, the word "inherited" was not intended to be used in its strict scientific sense. Certainly no violation of the laws of genetics was intended!

BENJAMIN L. GORDON, M.D.,
Atlantic City, N. J.

1616 Pacific Avenue.

1. Thucydides: History of the Peloponnesian War, book II, p. 47.

TRAUMATIC LIPORRHAGIA RETINALIS

To the Editor:—In my recent article "Traumatic Liporrhagia Retinalis (Verhoeff): Purtscher's Disease," which appeared in the March 1944 issue of the ARCHIVES, I inadvertently omitted from the bibliography reference to two important earlier articles both of which should have been included for specific and important reasons.

The first is the article by Bedell entitled, "Traumatic Retinal Angiopathy" (ARCH. OPHTH. **22:** 351-358 [Sept.] 1939), outstanding because of its exquisite color photographs of the fundus and because of its summary. The second is the article by Rados entitled, "Lymphorrhagia Retinae Traumatica" (ARCH. OPHTH. **6:** 93-103 [July] 1931). In the beautiful painting of the fundus in this article one can see that the white spots are contiguous to both arterioles and venules. Also, attention should be paid to Rados' comments in view of the recent term used for the condition, "traumatic liporrhagia retinalis." Other references have been uncovered, but these two articles should not have been overlooked.

EDMUND B. SPAETH, M.D., Philadelphia.

1930 Chestnut Street.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Cornea and Sclera

THE OCULAR CRITERIA OF DEFICIENCY OF RIBOFLAVIN. M. K. GREGORY, Brit. M. J. **2:** 134 (July 31) 1943.

The author criticizes the uncritical investigations and looseness in terminology which are encountered in discussions of the ocular changes associated with ariboflavinosis. He has selected one symptom, corneal vascularization, as it is generally recognized as a most characteristic sign and, according to some authors, it precedes all other demonstrable lesions of the deficiency. At the same time, Gregory would refrain from the diagnosis of a definite deficiency on the basis of this single change, with the absence of other signs, such as cheilosis and typical glossitis. The terms "circumcorneal injection" and "ciliary congestion" are indiscriminately used. It is necessary that the observer have an exact knowledge, first, of the normal blood supply and arrangement of the vessels at the limbus; second, of the changes which may be expected to occur, and third, of the other conditions which may produce a somewhat similar appearance and how these may be distinguished. The author describes the normal blood supply of the limbus. The chief sign of riboflavin deficiency is a superficial invasion of the cornea by fine capillaries arising from the apexes of the marginal loops. These lie just deep to the epithelium and extend evenly as streamer-like vessels which anastomose to form a series of loops. From the apexes of these loops more capillaries grow toward the center, giving the appearance with the slit lamp of fine, almost parallel, vessels extending on to the cornea around the whole of its periphery in both eyes. The extent of invasion may differ in the two eyes. Superficial and interstitial opacities develop at various stages but are of later occurrence than the initial vascularization. In cases of more advanced deficiency the vessels penetrate to a greater depth into the substantia propria. In a proportion of cases there is some injection of the pericorneal plexus, the injection in cases of mild deficiency being confined to the superficial layer of the conjunctiva. This condition is to be distinguished from other forms of corneal vascularization, such as occur in interstitial keratitis, vitamin A deficiency, pannus and any superficial keratitis.

The author examined 1,059 presumably normal persons for signs of riboflavin deficiency. Of these, 31 showed corneal vascularization, and of the latter, only 5 complained of any subjective symptoms, 4 presented slight disturbance of vision and 8 had other signs of riboflavin deficiency. A fuller report on these subjects will be published later. It was observed that after the administration of nicotinic acid, injection of the perilimbic plexus was observed in a few persons. The author believes that the local effect of these doses of nicotinic acid is important only within two hours of its administration.

ARNOLD KNAPP.

General Diseases

MOLLUSCUM CONTAGIOSUM OF THE EYE, ITS CLINICAL COURSE AND TRANSMISSIBILITY, AND THE CULTIVABILITY OF THE VIRUS. L. A. JULIANELLE and W. M. JAMES, Am. J. Ophth. **26:** 565 (June) 1943.

Julianelle and James state, on the basis of experimental evidence, that molluscum contagiosum of the eye was not transmitted to the monkey, rabbit or white mouse. Implantation of the virus in the hen egg, however, was followed in 2 of 4 experiments by infection of the chorioallantoic membrane, multiplication of the virus and appearance of typical inclusion bodies.

In conclusion, therefore, it may be said that molluscum contagiosum of the eye is an uncommon condition of the eyelids, characterized by persistent conjunctivitis, sometimes complicated by keratitis. The clinical appearance may be deceiving because of its similarity to that of marginal chalazions, milia and warts. Diagnosis by histologic examination is infallible and may be readily accomplished, since all nodules should be removed in any case as the logical and successful means of treatment. Molluscum contagiosum differs from most virus diseases in that the degree of infectivity is low. The observations which readily support this statement may be stated as follows: The process remains monocular; the infection does not spread readily to members of the family; even the intimate contact provided by wrestling does not cause dissemination of the infection among members of the same squad, and the infectious agent or virus has been propagated on chorioallantoic egg membrane in 2 of 4 attempts. W. ZENTMAYER.

THE OPHTHALMOSCOPE IN CLINICAL MEDICINE. A. MAITLAND RAMSAY, Brit. M. J. **1:** 685 (June 5) 1943.

Ramsay first pleads for the importance of clinical observation, with its personal training of the eyes and hands, which cannot be replaced

by mechanical apparatus and laboratory investigations. The best results are obtained by cooperation; the clinical examination should be exhausted by every means at its disposal before one calls on the laboratory, with full knowledge of the kind of assistance which is required from the laboratory worker. The interior of the living eye can be compared to a fully equipped biochemical laboratory by which one can study vital processes, so that the routine use of the ophthalmoscope by the physician is essential in every case. To understand the ophthalmoscopic findings, the microscopic anatomy of the eyeground must be known.

The address is limited to the ocular manifestations of the injurious effects of disordered metabolism on the cardiorenal system. The first sign of disease apparent in the eyeground is diminution or loss of transparency of the retina. Hypertension does not lead to rupture and hemorrhage so long as the vascular walls remain healthy; increase of blood pressure in late middle life may be the result of a hereditary predisposition, and, according to Ellis, in 90 per cent of cases it is benign. An upset in the physiologic ratio between systolic and diastolic blood pressure leads to hemorrhages from the capillaries of the retina. A disturbed ratio is much more serious than far higher hypertension with a normal ratio. Malignant hypertension is generally accompanied by some form of Bright's disease, and death occurs in a year from uremia.

One of the earliest signs of pathologic high blood pressure is constriction in the caliber of some of the branches of the retinal artery; the degree of the constriction is a guide to the severity of the systemic hypertension. The artery is straightened, and the presence of spasmodic constriction indicates hypertension. Loss of transparency of the vessel wall is another early sign; the outline of the wall then becomes clearly visible.

The earliest signs of arteriosclerosis are often seen in the eye. Gunn has shown that the arteries are irregularly contracted and tortuous, with an increased central light streak. The artery loses its transparency and becomes hard and rigid at such points as where it crosses a vein. In most cases the true essence of retinal hemorrhage is capillary dysfunction, rather than the action of increased blood pressure on a sclerosed artery.

Finally, the author recapitulates the three most important clinical types of retinitis: (1) arteriosclerotic, (2) albuminuric and (3) diabetic; they are easily differentiated by examination of the urine.

In conclusion, Ramsay states that the vascular changes in the eyeground are of value in the prognosis of general disease only when they are correlated with such symptoms of general disease as high blood pressure, albuminuria, glycosuria, uremia and anemia. The debt which general medicine owes to ophthalmology cannot be fully appreciated until the physician examines the eye with the ophthalmoscope as habitually as he feels the pulse, examines the heart and lungs and applies chemical and microscopic tests to the urine. ARNOLD KNAPP.

Glaucoma

IS GLAUCOMA A DEFICIENCY DISEASE? IMPORTANT DETAILS CONCERNING THE NONSURGICAL TREATMENT OF GLAUCOMA SIMPLEX. M. J. SCHOENBERG, Am. J. Ophth. **26:** 1282 (Dec.) 1943.

Schoenberg gives the following summary:

"The guiding principles in the treatment of glaucoma simplex are: (*a*) to eliminate or alleviate disturbances due to ill health; (*b*) to advise patients repeatedly about ways of maintaining good health; (*c*) to determine the stage and type of glaucoma, the age and type of the patient, and to treat accordingly; (*d*) to learn more about the mode of action of the drugs used in the local treatment of glaucoma, the frequency of application, dosage, intentional interruptions of treatment, timing, and combination of drugs; (*e*) pay utmost attention to minutest details; (*f*) to think always along clinical lines; to consider the probability that glaucoma is a deficiency disease."

W. S. REESE.

Lens

VENESECTION IN A CASE OF CHOROIDAL HEMORRHAGE FOLLOWING CATARACT EXTRACTION. J. J. REGAN, Am. J. Ophth. **26:** 534 (May) 1943.

A man aged 56 had had an operation on the left eye for cataract three years before and a later enucleation because of hemorrhage. He had had diabetes and arterial hypertension for the past three years. The patient was placed under treatment for his general condition, and about nine months later the right eye was operated on for cataract. On completion of the operation, blood was observed coming from below the iris near the surgical coloboma. The internist withdrew 22 ounces (660 cc.) of blood from a vein in the arm. Twenty-six hours later no intraocular hemorrhage was present. Later a discission was performed, with ultimate vision of 20/20 +. W. ZENTMAYER.

A COLORED REFLEX FROM THE ANTERIOR CAPSULE OF THE LENS WHICH OCCURS IN MERCURIALISM. W. S. ATKINSON, Am. J. Ophth. **26:** 685 (July) 1943.

Atkinson reports the observation with the slit lamp of a brownish reflex from the anterior capsule of the lens of persons with chronic mercurialism and of those who have worked for a

long time with mercury or in an atmosphere containing mercury, although they may exhibit no symptoms of mercurialism. The apparent haziness of the anterior capsule and the colored reflex do not interfere with vision. A similar colored reflex was observed from the anterior nuclear zone of the adult lens. The cornea did not exhibit the colored reflex, and no endothelial changes were noted. By oblique illumination the lenses of these eyes present a dull gray appearance. The colored reflex from the lens is suggested as a permanent, and probably an early, diagnostic sign of chronic mercurialism.

The article is well illustrated.

W. ZENTMAYER.

Methods of Examination

MALINGERING TESTS. J. O. WETZEL. Am. J. Ophth. **26:** 577 (June) 1943.

The visual defects most commonly simulated by draftees are complete blindness of one eye, notable lessening of vision in one or both eyes and, less frequently, accidental injury, either immediate or remote, resulting in inability to meet the standard for vision set for enlistment in the armed forces. Total blindness is seldom simulated, for the average draftee realizes that inquiry into his past history would soon unmask the fraud. Ingenious persons may devise more subtle deceptions, but their very unusualness will in most cases permit prompt detection.

Wetzel then describes the most practical effective tests for malingering that have been proposed. A chapter on simulated night blindness concludes the article. W. ZENTMAYER.

SPECIFICATIONS FOR DARK-ADAPTATION TESTS. K. J. W. CLARK, Brit. M. J. **1:** 632 (May 22) 1943.

A CRITIQUE OF THE BISHOP HARMAN TEST FOR NIGHT VISION. JOHN YUDKIN and ANDREW FERGUSON, ibid. **1:** 633 (May 22) 1943.

NIGHT-VISION TESTS. N. BISHOP HARMAN, ibid. **1:** 736 (June 12) 1943.

Dr. Craik speaks of two aspects of the problem of the exact specification of the light used in adaptometers, namely, standardization and calibration. With regard to Major Rycroft's paper on army tests for night vision, he draws attention to the fact that the pentagon was originally designed as a multiple, or group, test for examining five men simultaneously, but individual testing proved superior in practice. A neutral wedge is almost the ideal method of light control.

An investigation of the Bishop Harman apparatus was made with a view to determination of its efficacy as an instrument for the measurement of dark adaptation. It has been shown that, in addition to many theoretic objections, the test is unsatisfactory in practice as compared with well standardized apparatus, since other factors than dark adaptation are involved.

In a reply to the preceding articles, Harman claims that the objections to his method are those of pure research workers and that, though their work is impressive, they write wholly from the point of view of the laboratory. The author, like the majority of ophthalmic medical practitioners, on the other hand, must have a test which is designed to meet solitary needs.

The test should be so simple that any one can make it himself and obtain a reasonably accurate reaction. Harman continues to claim that he has used this test in a variety of places and has found that it worked well in all. The apparatus is of light weight, is easily carried and is independent of any wired connections. He found that fifteen minutes was generally useful for adaptation to darkness. Any one who failed to pass the test at a distance of 5 meters was given a double time. But the examinees who showed a gain with such extra time were few.

ARNOLD KNAPP.

Neurology

OCCLUSION OF THE ANTERIOR INFERIOR CEREBELLAR ARTERY. R. ADAMS, **49:** 765 (May) 1943.

The clinical and pathologic observations in a case of thrombosis of the anterior inferior cerebellar artery are presented. This syndrome is distinct from that which follows thrombosis of the posterior inferior or the superior cerebellar artery. Partial occlusion of the anterior inferior cerebellar artery is undoubtedly more common than has been believed, and it is expected that some of the distinctive features of this syndrome will permit its identification.

A table on syndromes resulting from occlusion of the cerebellar arteries is included. The clinical signs of thrombosis of the superior cerebellar artery are as follows: (1) homolateral: cerebellar asynergia, involuntary choreiform movements and Horner's syndrome; (2) contralateral: loss of pain and temperature senses over the face and body, sometimes partial deafness and sometimes weakness of the face of central type. The clinical signs of thrombosis of the anterior inferior cerebellar artery are as follows: (1) homolateral: cerebellar asynergia, Horner's syndrome, deafness, complete paralysis of the face, loss of pain and temperature senses over the face and diminished sensibility to light touch over the face; (2) contralateral: incomplete loss of pain and temperature senses over the body. The clinical signs referable to the posterior inferior cerebellar artery are as follows: (1) homolateral: cerebellar asynergia, Horner's syndrome, loss of pain and temperature senses over the face, dysphagia and dysphonia; (2) contralateral: loss of pain and temperature senses over the body.

R. IRVINE.

Ocular Muscles

AN OPERATION FOR THE CORRECTION OF PARALYTIC LATERAL-RECTUS PALSY. B. F. PAYNE, Am. J. Ophth. **26:** 390 (April) 1943.

The cases reported demonstrate two types of operation performed for paralysis of the lateral rectus muscle. In the first case a transplantation of the lateral halves of the tendons of the superior and inferior rectus muscles, with recession of the medial rectus muscle, was performed. In the second case, a simple resection and recession gave excellent results. In the latter case the situation was more favorable in that the paralysis had existed a shorter time and was specific in type. In the first case, about four and a half months after operation, with correcting glasses containing both lateral and vertical prisms, an abduction of 43 degrees on the perimeter was noted. Annoying diplopia was still present in the upper and lateral fields of gaze. In the second case, about four and a half months after the operation the patient had third grade fusion, with an amplitude of 5 degrees with the prism base in and of 35 degrees with the prism base out. The diplopia had disappeared.

W. ZENTMAYER.

Refraction and Accommodation

A STUDY OF THE ANISEIKONIA IN A CASE OF INCREASING UNILATERAL INDEX MYOPIA. H. M. BURIAN and K. N. OGLE, Am. J. Ophth. **26:** 480 (May) 1943.

Burian and Ogle reach the following conclusions:

"1. The clinical and analytic study of a case of increasing unilateral myopia due to nuclear sclerosis of the crystalline lens demonstrates the fact that refractive anisometropia is accompanied by aniseikonia.

"2. This case is contrasted with one having a similar degree of anisometropia not due to a unilateral nuclear sclerosis of the crystalline lens. No significant image-size difference was measured in the second case and the clinical evidence tended to show the myopia to be axial in nature. Thus it was pointed out that no a priori conclusions can be made as to the aniseikonia present in any given case of anisometropia.

"3. Finally, it is shown that the measurements obtained with the standard eikonometer (and space-eikonometer) are not measurements of the differential ocular movements caused by the prismatic effect of the lenses correcting the anisometropia."

W. ZENTMAYER.

Retina and Optic Nerve

PIGMENTARY DEGENERATION OF THE RETINA AND NERVE TYPE OF DEAFNESS. W. A. SIRLES and H. SLAUGHTER, Am. J. Ophth. **26:** 961 (Sept.) 1943.

The authors give the following summary:

"In the 12 cases of retinitis pigmentosa presented 6, or 50 per cent of the patients, showed varying degrees of deafness by audiometric examination.

"All cases of deafness were of the nerve type.

"Two of six patients who were deaf gave no history of impaired hearing.

"There was no demonstrable relationship between the onset of severity of the eye and ear symptoms.

"It is suggested that a common germ-plasm defect is present in the anlage of the inner ear and the retina."

W. ZENTMAYER.

Uvea

PIGMENT FRECKLES OF THE IRIS (BENIGN MELANOMAS): THEIR SIGNIFICANCE IN RELATION TO MALIGNANT MELANOMA OF THE UVEA. A. B. REESE, Am. J. Ophth. **27:** 217 (March) 1944.

Reese draws the following conclusions from a study of malignant melanoma.

"A malignant melanoma of the uvea may be accompanied by a single or by multiple benign melanomas. Such instances represent multiple origin of the tumor, and the iris is a common site for the benign feature. When the iris lesion is seen clinically it is a diagnostic aid."

W. S. REESE.

CHOROIDAL DETACHMENT. B. W. RYCROFT, Brit. J. Ophth. **27:** 283 (July) 1943.

Rycroft reviews the literature on detachment of the choroid. No mention is made of the articles by O'Brien (Detachment of Choroid After Cataract Extraction, ARCH. OPHTH. **14:** 527 [Oct.] 1935; Further Observations on Detachment of Choroid After Cataract Extraction, ibid. **16:** 655 [Oct.] 1936), in which it is stated that ophthalmoscopic examination of the fundus was attempted immediately after cataract extraction in 140 consecutive uncomplicated cases. In 92 of the cases the fundus was well visualized, and in 86 of these 92 cases detachment of the choroid was observed—an incidence of over 93 per cent.

In Rycroft's series, cataract extraction, either of the intracapsular and of the extracapsular type, was done in 60 cases, and a trephination was carried out in 80 cases. In 6 cases iridectomy was done for subacute glaucoma. The routine procedure was to examine the fundus within forty-eight hours after the operation. In 2 cases detachment of the choroid, of the immediate type, was noted after cataract extraction of the extracapsular type. In 18 of the 80 cases in

which trephination was carried out, detachment of the choroid appeared three days after operation. In 4 cases of acute glaucoma no detachment of the choroid was noted after broad iridectomy. In 1 case of absolute glaucoma experimental trephination was done, and detachment of the choroid was produced by subchoroid hemorrhage.

The author concludes that detachment of the choroid is primarily due to a forward movement of the diaphragm, consisting of the ciliary body, the suspensory ligament and the lens. He feels that the depth of the anterior chamber is the determining factor in the appearance of this complication after trephination. It is more likely to occur in the cases of chronic glaucoma in which the anterior chamber is deep, with allowance for a greater forward movement of the iris-lens diaphragm.

The most satisfactory form of treatment seems to be associated with closure of the fistula in the conjunctival flap.

The article is illustrated.

W. ZENTMAYER.

Therapeutics

QUALITIES AND LIMITATIONS OF PROFLAVINE. ARNOLD LAWSON, Brit. M. J. **1:** 229 (Feb. 12) 1944.

The author draws attention to a misunderstanding of the limitations of proflavine, which he considers a most useful and nonirritating antiseptic. He has used proflavine extensively and found it to be the most efficient and satisfactory antiseptic as a routine dressing in all ophthalmic operations. Its great value lies in its strong bactericidal qualities, coupled with its being completely painless and nonirritating. It is used in a strength not exceeding 1 : 2,000, and the solution is sprinkled freely on the gauze dressing. On completion of the operation the eye is irrigated with this solution before the dressing is applied. The author believes that thereby he avoids contamination from the lash area. As proflavine is an antiseptic in the true sense of the word, it is not to be employed when infection is present and should not be used in cases of acute purulent or semipurulent inflammation. Its usefulness is not in a direct ratio to the strength of the solution, and there is no advantage in using the solution stronger than 1 : 1,000; even at that concentration it is liable, if used continuously over more than a short period, to inhibit the healing of the wound. Its combination as a powder with sulfathiazole is contraindicated. In short, proflavine cannot be surpassed when the object is to prevent contamination from an outside source, but it is inferior to other remedies when a widespread infection is present. Acriflavine seems to be just as efficacious as proflavine in its antiseptic properties, but it is apt to cause irritation.

ARNOLD KNAPP.

News and Notes

EDITED BY DR. W. L. BENEDICT

PERSONAL NEWS

Leslie Dana Medal for the Prevention of Blindness.—The Leslie Dana Medal for the Prevention of Blindness has been awarded to Miss Linda Neville, Lexington, Ky.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION ON OPHTHALMOLOGY

FRANK C. KEIL, M.D., *Chairman*

WILLIS S. KNIGHTON, M.D., *Secretary*

March 20, 1944

Diagnosis of Diseases of the Inner Portion of the Eye. DR. ARNOLD KNAPP.

As a result of advances in laboratory and clinical tests and a better correlation with general medicine, the ophthalmologist is enabled to obtain valuable information in cases of diseases of the inner part of the eye in which diagnosis is difficult or the course is atypical. The following conditions illustrate the point.

Sarcoidosis.—A man aged 22 complained of redness of the eyes and failing vision for five months. Vision was 20/200 in the right eye and 2/70 in the left eye. The eyes were moderately congested; there were posterior corneal deposits, irregular pupils with numerous adhesions and clusters of grayish, translucent and vascularized nodules, which seemed to be partly in the stroma of the iris and partly in the anterior chamber. The fundus reflex was seen, but there were do details. Roentgenographic examinations showed glandular enlargement about the hilus of the lungs, with peribronchial thickening, and characteristic changes in the terminal phalanges. Biopsy of an enlarged epitrochlear gland revealed the histologic changes characteristic of sarcoidosis; epithelioid cells resembling those seen in tubercles, absence of caseation and occasional giant cells.

The eyes were treated with roentgen rays, but the process progressed; because of secondary glaucoma an iridectomy was performed, and some of the nodular mass in the iris was removed. Microscopic examination revealed changes similar to those present in the epitrochlear gland. The condition of the eyes became steadily worse and ended in shrinkage of the eyeballs.

Brucellosis.—In the first case a boy aged 10 years gave a history of slight inflammation of the eyes for three weeks, without apparent cause. Vision was 20/30 in the right eye and 20/70 in the left eye. The most striking symptom was well marked corneal deposits, with neuroretinitis in the left eye. General examination revealed nothing significant. In the hospital the patient had an afternoon fever. Both the cutaneous and the opsonophagocytic test for brucellosis gave positive results.

In the second case, a woman aged 30 had vision of 20/200 in the right eye and of 20/30 in the left eye. There were atrophic areas in the choroid of both eyes. These areas were unusually white, and the pigment was in massive clumps. The general physical examination had revealed nothing significant. Both cutaneous and the opsonophagocytic test for brucellosis gave positive results.

Toxoplasmosis.—An infant aged 10 weeks was seen on March 29, 1940. Directly after birth it was noted that the child did not follow the light with its eyes. There had been no illness, and the infant seemed to be in fairly good physical condition. Examination of the fundus showed a white mass with hemorrhagic areas and choroidal changes in the right eye and subretinal exudates and atrophic choroidal spots in the left eye. A diagnosis of glioma retinae had been made, but the ophthalmoscopic picture seemed to differ from the condition observed in cases of glioma, as did the history. In 1941 the child developed normally and remained in good physical condition. No particular changes occurred in the eyegrounds. The child did not sit up, and pressure on the brain was suspected. Examination was made at the Neurological Institute by Dr. Abner Wolf and Dr. F. L. P. Koch, who expressed the belief that the child had toxoplasmic encephalomyelitis.

In 1942 the child continued to develop, and the eyegrounds showed chorioretinal changes and formation of connective tissue in the vitreous. The pupils did not react, and there was apparently no vision. The parents reported on Sept. 24, 1943 that the child was doing well and was thought to have good mentality, but spasticity had developed in the left leg.

Although the diagnosis is far from certain, this case suggests that when glioma is suspected, but the process does not run the usual course and there are no advances in the fundic picture, the possibility of toxoplasmosis should be borne in mind and the following procedure carried out: A careful history of early life should be obtained, and roentgenographic and ventriculographic studies of the head, examination of the spinal fluid and serologic tests should be made.

Evaluation of Advances in Ophthalmic Surgery. DR. JOHN H. DUNNINGTON.

It is difficult to determine what constitutes a recent advance in ophthalmic surgery, for both time and experience are necessary for a correct

appraisal of the worth of a procedure. A few of the generally accepted changes that have occurred in ophthalmology within the past decade or so are indicated.

Such fairly recent safeguards as preoperative sedation, akinesia and retrobulbar injection are routine today and head the list of "musts" in intraocular surgery. Solution of tribromoethanol U. S. P. and pentothal sodium have proved their usefulness in ophthalmic operations.

The technic of dacryocystorhinostomy for chronic dacryocystitis has been improved to a point at which drainage can be established in most instances, and encouraging results have also been obtained in cases of annoying epiphora following extirpation of the lacrimal sac. One is no longer justified in excising the sac in all cases in which relief is not obtained by probing.

Today corneal grafting is a recognized surgical procedure, the technical details of which are still in the process of evolution. The degree of vascularization of the opaque cornea seems to be the most important single factor in determining the subsequent fate of the graft. Removal of the major portion of highly vascularized scar gives promise of being of more value than irradiation in reduction of later infiltration with blood vessels.

In the field of glaucoma surgery, the importance of early operative intervention has been stressed by many authors. In a five year follow-up study of 105 patients, Reese found that the condition was arrested in 90 per cent of patients operated on early in the disease and in only 28 per cent of patients with late manifestations. There has been a decided trend toward some operation for inclusion of the iris, although it is not a new procedure. The first principle of good surgery, viz., simplicity, holds here.

Within the past decade, at least two accepted changes have occurred in the technic of cataract extraction. The first is the corneoscleral suture. The whole process has as its underlying principle healing by primary intention. With proper suturing there is an increased frequency of early restoration of the anterior chamber, which does so much to prevent postoperative glaucoma. The method of placing the suture and the most favorable composition of the suture itself, whether of silk or of an absorbable material, are still matters of debate. The second change is in the intracapsular extraction. The increased use of this operation can be attributed to many factors, such as akinesia, retrobulbar injection and use of corneoscleral sutures. The method of delivering the lens in its capsule still varies, but the tendency is toward a greater use of the capsule forceps to steady the lens while it is being dislocated and expressed by the hook, i. e., the employment of less pull and more push. There is a decided trend toward preservation of the iris sphincter—the so-called extraction with round pupil.

The most sensational surgical development within the past twenty years has been the treatment of retinal detachment. While the percentage of successful results is increasing, it could be larger if surgeons paid more attention to the important details, such as careful localization of the retinal tear, instead of treating the entire affected area—a mistake which, fortunately, is becoming much less frequent. Closure of the tear and adhesion of the retina around the hole are today the accepted principles of operation for detachment. The trend is toward more surface applications, with fewer perforations. It is essential, however, to use a sufficient number of perforations so that the retina will be in proper position at the close of the operation. Excessive treatment should be avoided, for it leads to massive scarring in the retina and predisposes to the development of a severe intraocular hemorrhage.

Diagnosis of Abnormalities of the Extraocular Muscles and Their Surgical Treatment. Dr. James W. White.

Experience at the Post-Graduate Hospital has proved the value of two procedures in the surgical treatment of extraocular muscles: (1) operation on the inferior oblique muscle at its insertion, and (2) use of the manner of fixation as a guide to the choice of operation in cases of strabismus.

Operation on the inferior oblique muscle at its insertion was first performed at the Post-Graduate Hospital in 1936 and has gained in favor constantly wherever it has been tried. The operation is safer than when performed at the origin of the muscle, where the inferior rectus muscle may be injured by mistake.

The action of the inferior oblique muscle may be decreased by a recession at its insertion or may be increased by tucking or splicing. The indications and technic are fully covered in the literature.

The use of fixation as a guide to the choice of operation is a principle enunciated by Duane.

When the squinting eye is amblyopic, it should be straightened by shortening one muscle and weakening its direct antagonist. The major effect should be secured by operation on the deviating eye alone, the procedure being kept within reasonable limits. If this proves inadequate, the same procedure should be carried out on the other eye, care always being taken to preserve a normal near point of convergence.

But when the esotropia is alternating, two conditions may be encountered: In one type the right eye fixes in the primary position and in the position of eyes right, and the left internal rectus muscle is overacting. A similar overaction of the right internal rectus muscle takes place when the left eye fixes in front and to the

left. The esotropia is usually less for distance than for near vision. Both internal rectus muscles are very strong, and bilateral tenotomy or recession gives a good result.

The other type of esotropia is seen when vision of the poorer eye is only slightly reduced. The esotropia is about the same for distance as it is for near vision and may be freely alternating, or with only slight preference for one eye. The right eye may fix in the position of eyes front or of eyes left, while the fellow eye fixes in the position of eyes front and in that of eyes right. In this type neither external rectus muscle is used to abduct the eye, since the fellow eye is fixating in the nasal field. This condition leads in time to a functionally underacting external rectus muscle of each eye and accounts for the similarity in the esotropia for distance and for near vision. The internal rectus muscles are not spastic, since they are used to fixate in their respective nasal fields. In cases of this type the external rectus muscles should be shortened, but the weakening of the internal rectus muscles should be done most carefully, since here a remote near point of convergence is more frequently seen and weakening may lead to exotropia. In cases of exotropia similar variations are present.

With muscle paralyses, either congenital or of some duration, the choice of the fixating eye is of equal, or even greater, importance. In cases of acute paralysis the fixation in the field of the paretic muscle is so unstable that the necessary uncertainty causes the preference for fixation with the nonparetic eye. There are notable exceptions to this rule, as to all rules for anomalies of the extraocular muscles.

In cases of unilateral or bilateral paralysis of the superior rectus muscle, when fixation is preferred by either eye in the field of action of its paretic superior rectus muscle, there is a pronounced secondary deviation of the fellow eye. Here a recession of one or both inferior oblique muscles is indicated. However, if the left eye fixates in the position of eyes right and of eyes up and to the left, there is no secondary deviation of the other eye, except as brought out by the screen comitance test. Shortening of the superior rectus muscles is indicated.

Paralyses of both elevator muscles of one eye are divided into three types: first, the type in which binocular single vision is maintained by backward tilting of the head; second, the type in which fixation is maintained by the nonparetic eye, with the paretic eye in the position of primary deviation. When the vision of the hypotropic eye is fairly good, it may be found to fixate objects in the lower field, while the nonparetic eye fixates in the primary position and in the upper field of vision. The ptosis in this type of paralysis may be true or false. In the third type of paralysis fixation is preferred by the eye having the paretic muscles. In this type there is pronounced secondary deviation of both elevator muscles of the nonparetic eye.

The surgical procedure indicated in cases of the first two types is shortening of the paretic muscles, while in cases of the third type recession or tenotomy must be done on both elevator muscles of the nonparetic eye. In cases of all three types the eyes should be made at least cosmetically level before any operation for associated true ptosis is attempted.

When the superior oblique muscle is paretic and fixation is made with the nonparetic eye, a secondary contracture of the inferior oblique muscle of the paretic eye develops. But if the paretic eye fixates, there is little, or no, secondary contracture of the inferior oblique muscle, but a pronounced secondary deviation develops in the inferior rectus muscle of the nonparetic eye.

The problem becomes more complex when the nonparetic eyes fixates in some directions of gaze and the paretic eye is used in other fields.

Chemical Burns of the Eyes. Dr. William F. Hughes Jr., Baltimore.

Ocular injuries by a number of chemical agents produce lesions with many similar characteristics, namely: rapid penetration into the ocular tissues, with resulting cellular necrosis; a polymorphonuclear response within a few hours; conjunctival and corneal edema; iritis; vascularization of the cornea within five to eight days, and varying amounts of corneal infiltration and ulceration, which are repaired by the proliferation of opaque fibrous tissue.

Acid Burns.—These burns are nonprogressive, and the precipitation of the corneal proteins by acid is closely dependent on the character of the anion.

Alkali Burns.—These injuries, which are progressive in type, resemble burns with vesicant war gases. The relapsing tendency has been attributed to loss of corneal mucoid, precipitation of calcium salts and necrosis of blood vessels at the limbus. Treatment consists of (1) immediate removal of residual alkali by irrigation with water or a buffer solution (e. g., a 0.05 molar solution of acetic acid or a 0.05 molar solution of sodium acetate), (2) instillation of atropine, (3) measures to promote healing of the corneal ulceration and (4) prevention of symblepharon. The beneficial effects of ammonium salts or the emergency removal of necrotic conjunctiva, with replacement by oral mucous membrane (Denig graft), have not been adequately demonstrated.

Mustard Gas (dichloroethyl sulfide).—Although mild ocular burns were common in World War I, devastating or recurrent corneal lesions were rare (0.1 per cent of casualties). Since mustard gas disappears from the cornea before the victim is aware of having been ex-

posed to mustard gas vapor, decontamination is impossible. After splash burns, irrigations are of value if performed within three minutes after exposure. Later treatment is directed toward the prevention of secondary complications, such as iritis, corneal ulceration and secondary infection.

Lewisite (dichlorobetachlorovinylarsine).—The vapor or liquid produces excruciating ocular pain and blepharospasm immediately. As compared with the mustard action of gas, tissue necrosis and exudation are more intense. Treatment consists of a single instillation of about 0.1 to 0.5 cc. of special anti-lewisite ointment immediately after exposure.

Simultaneous Local Application of Penicillin and Sulfacetimide. DR. L. VON SALLMANN.

This paper was published in the September 1944 issue of the ARCHIVES, page 190.

Rehabilitation of the War Blinded. DR. MERLE E. FRAMPTON.

"The fear of blindness is the fear of utter darkness, the fear of restricted activity or helplessness, a fear of the future with the loss of earning capacity, the fear of loneliness and of being placed by one's friends in a world apart." One must recognize and understand these fears in order to help the newly blind to overcome them. Steps are already being taken by medical men, educators, industrialists and others for the proper rehabilitation, both medically and socially, of such blinded persons. However, all the conferences will be unproductive of results unless a carefully coordinated plan is drawn up to assure jobs in industry, as the only permanent therapeutic aid. A well planned program for the war blinded, if correctly developed, will aid all the civilian blind, who will have the same consideration under federal law as has the blinded veterans under the Veterans Administration Facility.

The first steps in the rehabilitation of the blind are, of necessity, the physical, mental and social adjustments, and these are preliminary to all permanent therapeutics. A basic principle, which must never be forgotten, is that the blind man should be reeducated in terms of adjustment to an active, normal working life in a real world. One should not look for permanent living or confinement in a sanatorium or institution, for idleness and broken morale will surely result. A further aim is the development of wide versatility in vocational and avocational directions as the keynote of all occupational rehabilitation. A blind man cannot do everything a man with normal sight can do, but he can do a great many things that he has not tried, or been given an opportunity to try. The government should assume the responsibility for finding or providing the man with the right job to assure permanent rehabilitation. Vocational education, or even retraining, is in itself not enough. The blind man must be adjusted to occupational opportunities and conditions in his home community. He has both an individual and a community adjustment to make.

The blinded war veterans will receive approximately $195 a month as a life pension, plus other considerations under the law. This financial status will, of itself, be a difficult hurdle to overcome in the rehabilitation program; it should not be allowed to weaken a man's morale or to become a deterrent to his seeking proper vocational adjustment. The highest form of therapeutics is self-respecting work in the right job.

Time is the all-essential factor in rehabilitation of any sort. With the blind it is more important than any other item. Delay demoralizes, deepens the fears and makes the process of rehabilitation much more difficult of accomplishment. It is imperative, therefore, that the program should begin with bedside therapy in the hospital. The present plan is to locate all blind patients at one center, with a program designed for medical therapy and a short period of social adjustment. This should meet the demand for immediate attention. The next step will be to place the man in his community, in a job, so that he may take his place once more as a self-respecting, productive citizen. It may involve a period of diagnostic study, retraining and apprenticeship. The development of this part of the plan is exceedingly difficult at present because of the failure of present governmental efforts to coordinate their programs. Until an agency with sole responsibility is secured, no sound program will be developed. This is too much to expect under the existing conditions of political structure, but one can continue to point out the necessary steps. Immediate mental and social adjustment service must be provided by experts at the hospital bedside. There must be further provided training and adjustment centers in cooperation with experienced private agencies serving the area. A plan of advisory services between the government and private agencies must be created, so that there will be no gaps in service. Such cooperative plans should cover, first, advisory vocational clinical service; second, the use of existing trained personnel; third, the use of existing plants and equipment, and, fourth, the vocational adjustment in the local community. There should be organized within the near future national surveys of industry, through the United States Office of Employment Service, to ascertain what jobs are available in private industry and with the government for the blinded man. The problem of convincing the employer of the

utility of blind labor is constantly one of major importance, and it is necessary to educate the public concerning its possibilities. At the New York Institute for the Education of the Blind my associates and I have developed a diagnostic clinic where we give each man a complete battery of mental, social and aptitude tests. We try to secure an adjustment profile for each person. This clinic acts likewise as a training clinic for all patients referred to it. The case worker is thus enabled to have a complete picture of the blind man before any attempt is made to complete his process of rehabilitation and placement. It took a war to demonstrate to industry and to the institutions designed to service the blind that blind men and women could find employment in normal industry. Many people whose condition comes within the definition of blindness are now working in industrial plants throughout greater New York and greater New Jersey. Nearly all these placements have been made without undue modification of the normal procedures in the industry concerned. Over 60 per cent of the workers were totally blind, and some were deaf as well.

Up to the present there are probably not more than 75 cases of blindness in the American forces as a direct result of the war, and it has been estimated that there will not be more than 500 cases if the war lasts five years. There will, therefore, be few blind men in one general area; they will be scattered over the country. Their rehabilitation and adjustment to ordinary community life constitutes an educational, medical and vocational problem, and all specialists are needed in a closely knit combat team if the objective is to be won.

Book Reviews

Light, Vision and Seeing. By Matthew Luckiesh, D.Sc., D.E., Director, Lighting Research Laboratory, General Electric Company, Cleveland. Price, $4.50. Pp. 323, with 16 illustrative plates and 83 figures in the text. New York: D. Van Nostrand Company, Inc., 1944.

One of the striking features of the industrial era has been its interest in sources of natural power and their relation to human activities and to society in general. This practical attitude has been mirrored in the progress of experimental science, with its basic method of controlled observation, in the study of phenomena which philosophers and metaphysicians of earlier days ignored or, at best, subjected to a critique of pure reason, speculation and deep thought at the sage's study table. This has been notably the case with that all-pervading and invaluable form of cosmic energy known as light. When studied in its applied form, analyzed, tested and standardized, it emerged as lighting, natural or artificial, and the science of illuminating engineering was born.

Dr. Luckiesh's book presents the subject of light and vision from this standpoint, and more pertinently in connection with the manifold purposes and requirements of science, industry and education in present day civilization. However, "Light, Vision and Seeing" is more than a simplification and condescending popularization of a subject which has implications in so many varied and widespread fields. As a result the author's presentation has the defects of its qualities. It offers a wealth of observational, experimental and critical data, analyzed well, documented and graphically illustrated, to be practically applied to everyday life and activities, as well as to many activities which are professional and technical. On the other hand, one might find fault with the rather diffuse, some would say unscientific, way in which a large number of disparate aspects and problems have been taken in hand. After some comment on the organ and function of sight and the status and science of lighting, there is an interesting review of milestones in lighting progress, of brightness, size and contrast as factors in vision, the time element, test charts and the meaning and measurement of visibility, brightness engineering, light and color, efficiency, safety and easy seeing. In a final chapter the author lists one hundred questions representative of those commonly asked and answers them briefly. The comprehensive index completes a work which will instruct and interest a large number of readers, both professional and lay, and prove of value as an authoritative handbook for reference.

PERCY FRIDENBERG.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Rua Consolacão, São Paulo, Brazil.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chengtu Ophthalmological Society

President: Dr. Eugene Chan.
Secretary: Dr. K. S. Sun.
Place: Eye, Ear, Nose and Throat Hospital, Chengtu, China.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. I. Imre, Budapest.
Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, Máriautca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

North of England Ophthalmological Society

President: Mr. John Foster, 45 Park Sq., Leeds.
Secretary: Mr. William M. Muirhead, 70 Upper Hanover St., Sheffield.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

Ophthalmological Society of Australia

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the secretary, Dr. Mohammed Khalil.

Ophthalmological Society of the United Kingdom

President: Mr. Charles B. Goulden, O.B.E., M.D., M.Ch., 89 Harley St., London.
Secretary: Mr. Frank W. Law, M.A., M.D., F.R.C.S., 30 Devonshire Pl., London W. 1.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

Oxford Ophthalmological Congress

Master: Mr. P. G. Doyne, 60 Queen Anne St., London, W. 1, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

Polish Ophthalmological Society

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

Royal Society of Medicine, Section of Ophthalmology

President: Col. F. A. Juler, 96 Harley St., London, W. 1, England.
Secretary: Dr. Harold Ridley, 60 Queen Anne St., London, W. 1, England.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

São Paulo Society of Ophthalmology

President: Prof. Moacyr E. Alvaro, Consolação 1151, São Paulo, Brazil.
Secretary: Dr. Silvio de Almeida Toledo, Enfermaria Santa Luzia, Santa Casa de Misericordia, Cesario Motta, St. 112, São Paulo, Brazil.

Scottish Ophthalmological Club

President: Dr. S. Spence Meighan, 13 Woodside Pl., Glasgow, C. 3.
Secretary: Dr. Alexander Garrow, 15 Woodside Pl., Glasgow, C. 3.
Place: Edinburgh and Glasgow, in rotation.

Sociedad Argentina de Oftalmologia

Chairman: Dr. Jorge Malbrán, Buenos Aires.
Secretary: Dr. Benito Just Tiscornia, Santa Fe 1171, Buenos Aires.

Sociedad Oftalmologia del Litoral, Rosario (Argentina)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.
Place: Rosario. Time: Last Saturday of every month, April to November, inclusive. All correspondence should be addressed to the President.

Sociedade de Oftalmologia de Minas Gerais

President: Prof. Hilton Rocha, Rua Rio de Janeiro 2251, Bello Horizonte, Minas Geraes, Brazil.
Secretary: Dr. Ennio Coscarelli, Rua Aimorés 1697, Bello Horizonte, Minas Geraes, Brazil.

Sociedade de Oftalmologia e Otorrinolaringologia de Rio Grande do Sul

President: Dr. Luiz Assumpção Osorio, Edificio Vera Cruz, Apartamento 134, Porto Alegre, Rio Grande do Sul.
Secretary: Dr. Fernando Voges Alves, Caixa Postal 928, Porto Alegre, Rio Grande do Sul.

Sociedade de Ophthalmologia e Oto-Rhino-Laryngologia da Bahia

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

Società Oftalmologica Italiana

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

Société Française d'Ophtalmologie

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

Society of Swedish Ophthalmologists

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 Ill tr., Stockholm, Sö.

Tel Aviv Ophthalmological Society

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

American Medical Association, Scientific Assembly, Section on Ophthalmology

Chairman: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
Secretary: Dr. R. J. Masters, 23 E. Ohio St., Indianapolis.
Place: Philadelphia. Time: June 18-22, 1945.

American Academy of Ophthalmology and Otolaryngology, Section on Ophthalmology

President: Dr. Lawrence T. Post, Metropolitan Bldg., St. Louis.
President-Elect: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.
Executive Secretary-Treasurer: Dr. William L. Benedict, 101-1st Ave. Bldg., Rochester, Minn.

American Ophthalmological Society

President: Dr. S. Judd Beach, 704 Congress St., Portland, Maine.
Secretary-Treasurer: Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y.

Association for Research in Ophthalmology, Inc.

Chairman: Dr. Conrad Berens, 35 E. 70th St., New York.
Secretary-Treasurer: Major Brittain F. Payne, School of Aviation Medicine, Randolph Field, Texas.
Assistant Secretary-Treasurer: Dr. Hunter Romaine, 35 E. 70th St., New York.

Canadian Medical Association, Section on Ophthalmology

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

Canadian Ophthalmological Society

President: Dr. R. Evatt Mathers, 34½ Morris St., Halifax, N. S.
Secretary-Treasurer: Dr. Kenneth B. Johnston, Suite 1, 1509 Sherbrooke St. W., Montreal.

National Society for the Prevention of Blindness

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

Academy of Medicine of Northern New Jersey, Section on Eye, Ear, Nose and Throat

President: Dr. N. Zwaifler, 46 Wilbur Ave., Newark.
Secretary: Dr. William F. Keim Jr., 25 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

Central Wisconsin Society of Ophthalmology and Otolaryngology

President: Dr. L. J. Friend, 425 E. Grand Ave., Beloit, Wis.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

New England Ophthalmological Society

President: Dr. Paul A. Chandler, 5 Bay State Rd., Boston.
Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

Pacific Coast Oto-Ophthalmological Society

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

Puget Sound Academy of Ophthalmology and Oto-Laryngology

President: Dr. L. L. Bull, 1215–14th Ave., Seattle, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle 1.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

Rock River Valley Eye, Ear, Nose and Throat Society

President: Dr. J. Sheldon Clark, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

Saginaw Valley Academy of Ophthalmology and Otolaryngology

President: Dr. M. H. Pike, Midland, Mich.
Secretary-Treasurer: Dr. H. H. Heuser, 207 Devidson Bldg., Bay City, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July, August and September.

Sioux Valley Eye and Ear Academy

President: Dr. J. C. Decker, 515 Francis Bldg., Sioux City, Iowa.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

Southern Medical Association, Section on Eye, Ear, Nose and Throat

Chairman: Dr. John H. Burleson, 414 Navarro St., San Antonio, Texas.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.

Southwestern Academy of Eye, Ear, Nose and Throat

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

Southwestern Michigan Triological Society

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

Western Pennsylvania Eye, Ear, Nose and Throat Society

President: Dr. Ray Parker, 218 Franklin St., Johnston, Pa.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

Arkansas State Medical Society, Eye, Ear, Nose and Throat Section

President: Dr. Raymond C. Cook, 701 Main St., Little Rock.
Secretary: Dr. K. W. Cosgrove, Urquhart Bldg., Little Rock.

Colorado Ophthalmological Society

President: Dr. C. A. Ringle, 912–9th Ave., Greeley.
Secretary: Dr. W. A. Ohmart, 1102 Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. F. L. Phillips, 405 Temple St., New Haven.
Secretary-Treasurer: Dr. W. H. Turnley, 1 Atlantic St., Stamford, Conn.

Eye, Ear, Nose and Throat Club of Georgia

President: William O. Martin Jr., Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. C. K. McLaughlin, 526 Walton St., Macon.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. J. K. Von Lackum, 117–3d St. S. E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

Kansas State Medical Society, Section on Ophthalmology and Otolaryngology

President: Dr. W. D. Pittman, Pratt.
Secretary: Dr. Louis R. Haas, 902 N. Broadway, Pittsburg.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. Val H. Fuchs, 200 Carondelet St., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Secretary: Dr. William A. Kennedy, 372 St. Peter St., St. Paul.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. William Morrison, 208 N. Broadway, Billings, Mont.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr B. E. Failing, 31 Lincoln Park, Newark.
Secretary: Dr. George Meyer, 410 Haddon Ave., Camden.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. Harold J. Joy, 504 State Tower Bldg., Syracuse 2.
Secretary: Dr. Maxwell D. Ryan, 660 Madison Ave., New York 21.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. Hugh C. Wolfe, 102 N. Elm St., Greensboro.
Secretary: Dr. Vanderbilt F. Couch, 104 W. 4th St., Winston-Salem.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. W. L. Diven, City National Bank Bldg., Bismarck.
Secretary-Treasurer: Dr. A. E. Spear, 20 W. Villard, Dickenson.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Neely, 1020 S. W. Taylor St., Portland.
Secretary-Treasurer: Dr. Lewis Jordon, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Pennsylvania Academy of Ophthalmology and Otolaryngology

President: Dr. Lewis T. Buckman, 83 S. Franklin St., Wilkes-Barre.
Secretary Pro Tem: Dr. Paul C. Craig, 232 N. 5th St., Reading.
Time: Last week in April.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. F. H. Rosebrough, 603 Navarro St., San Antonio.
Secretary: Dr. M. K. McCullough, 1717 Pacific Ave., Dallas.

Utah Ophthalmological Society

President: Dr. R. B. Maw, 699 E. South Temple, Salt Lake City.
Secretary-Treasurer: Dr. Charles Ruggeri Jr., 1120 Boston Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

West Virginia State Medical Association, Eye, Ear, Nose and Throat Section

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

Akron Academy of Ophthalmology and Otolaryngology

President: Dr. E. L. Mather, 39 S. Main St., Akron, Ohio.
Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.
Time: First Monday in January, March, May and November.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.
Acting Secretary: Dr. A. V. Hallum, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., fourth Monday of each month, from October to May.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. Michael J. Buonaguro, 589 Lorimer St., Brooklyn.
Secretary-Treasurer: Dr. Benjamin C. Rosenthal, 140 New York Ave., Brooklyn 16.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. Walter F. King, 519 Delaware Ave., Buffalo.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.
Secretary: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago.
Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati General Hospital Ophthalmology Staff

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.
Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.
Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

Cleveland Ophthalmological Club

Chairman: Dr. Shandor Monson, 1621 Euclid Ave., Cleveland.
Secretary: Dr. Carl Ellenberger, 14805 Detroit Ave., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Clerk: Dr. George F. J. Kelly, 37 S. 20th St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. H. D. Emswiler, 370 E. Town St., Columbus, Ohio.
Secretary-Treasurer: Dr. D. G. Sanor, 206 E. State St., Columbus, Ohio.
Place: The Neil House. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. C. B. Collins, 704 Medical Professional Bldg., Corpus Christi, Texas.
Secretary: Dr. L. W. O. Janssen, 710 Medical Professional Bldg., Corpus Christi, Texas.
Time: 6:30 p. m., third Tuesday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Ruby K. Daniel, Medical Arts Bldg., Dallas 1, Texas.
Secretary: Dr. Tom Barr, Medical Arts Bldg., Dallas 1, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Cecil W. Lepard, 1025 David Whitney Bldg., Detroit 26.
Place: Club rooms of Wayne County Medical Society.
Time: First Wednesday of each month, November to April, inclusive.

Detroit Ophthalmological Society

President: Dr. Raymond S. Goux, 545 David Whitney Bldg., Detroit 26.
Secretary: Dr. Arthur Hale, 1609 Eaton Tower, Detroit 26.
Place: Club rooms of Wayne County Medical Society. Time: 6:30 p. m., third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Appointed at each meeting.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. Rex Howard, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. R. H. Gough, Medical Arts Bldg., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Lyle J. Logue, 1304 Walker Ave., Houston, Texas.
Secretary: Dr. John T. Stough, 803 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Oto-laryngological Society

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.
Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.
Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. M. E. Trainor, 523 W. 6th St., Los Angeles.
Secretary-Treasurer: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time. 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.
Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.
Place: 1718 M St. N.W. Time: 8 p.m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p.m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. Leon H. Guerin, 324 E. Wisconsin Ave., Milwaukee 2.
Secretary-Treasurer: Dr. Frank G. Treskow, 411 E. Mason St., Milwaukee 2.
Place: University Club. Time: 6:30 p. m., fourth Tuesday of each month from October to May.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.
Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashvile, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May

New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St. New Haven, Conn.
Secretary: Dr. Frederick A. Wiess, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Oto-Laryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Thomas H. Johnson, 30 W. 59th St., New York.
Secretary: Dr. Wendell L. Hughes, 131 Fulton Ave., Hempstead, N. Y.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Milton Berliner, 57 W. 57th St., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Oklahoma City Academy of Ophthalmology and Otolaryngology

President: Dr. James P. Luton, 117 N. Broadway, Oklahoma City.
Secretary: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. D. D. Stonecypher, Nebraska City, Neb.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.
Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

President: Dr. Isaac Tassman, 136 S. 16th St., Philadelphia.
Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. George H. Shuman, 351-5th Ave., Pittsburgh.
Secretary: Dr. Robert J. Billings, 509 Liberty Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Reading Eye, Ear, Nose and Throat Society

President: Dr. Michael J. Penta, 312 N. 5th St., Reading, Pa.
Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.
Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from September to July.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. Peter N. Pastore, Medical College of Virginia, Richmond, Va.
Secretary: Dr. Clifford A. Folkes, Professional Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

St. Louis Ophthalmic Society

President: Dr. C. C. Beisbarth, 3720 Washington Blvd., St. Louis.
Secretary: Dr. H. R. Hildreth, 508 N. Grand Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting, 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmo-Oto-Laryngological Society

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.
Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.
Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Roy H. Parkinson, 870 Market St., San Francisco.
Secretary: Dr. A. G. Rawlins, 384 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Clarence A. Veasey Sr., 421 W. Riverside Ave., Spokane, Wash.
Secretary: Dr. Clarence A. Veasey Jr., 421 W. Riverside Ave., Spokane, Wash.
Place: Spokane Medical Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. A. H. Rubenstein, 713 E. Genesee St., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. E. W. Campbell, 316 Michigan St., Toledo, Ohio.
Secretary: Dr. L. C. Ravin, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. S. Bockoven, 1752 Massachusetts Ave., Washington, D. C.
Secretary-Treasurer: Dr. John Lloyd, 1218–16th St. N. W., Washington, D. C.
Place: Medical Society of District of Columbia Bldg., 1718 M St. N. W., Washington, D. C. Time: 7:30 p. m., first Monday in November, January, March and May.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.